

Enantioselective Benzylation and Allylation of α -Trifluoromethoxy Indanones under Phase-Transfer Catalysis

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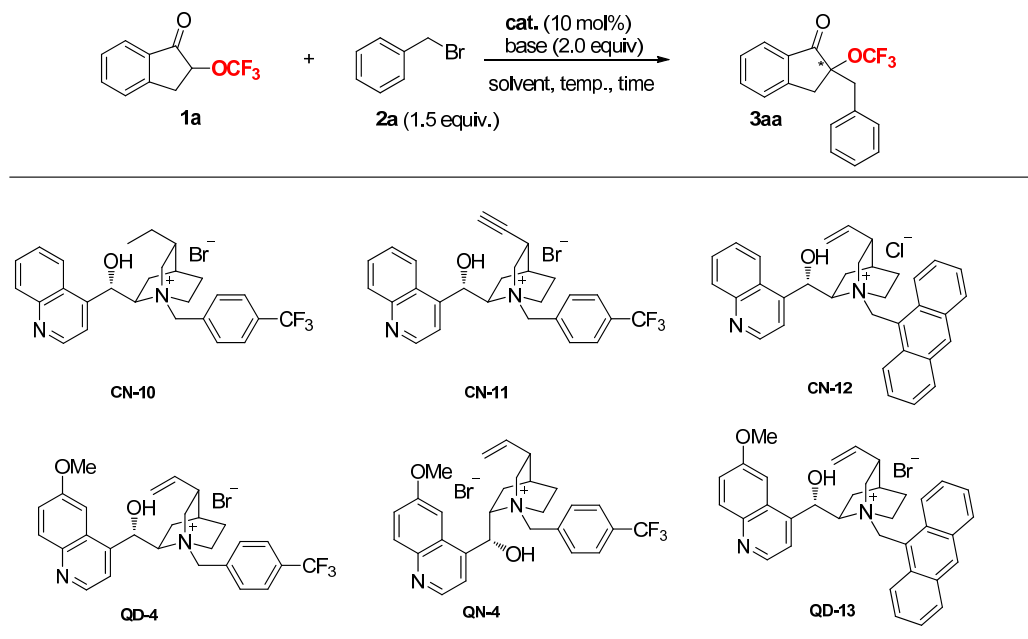
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1. Optimization of Reaction Condition

Table S1. Optimal condition screening ¹

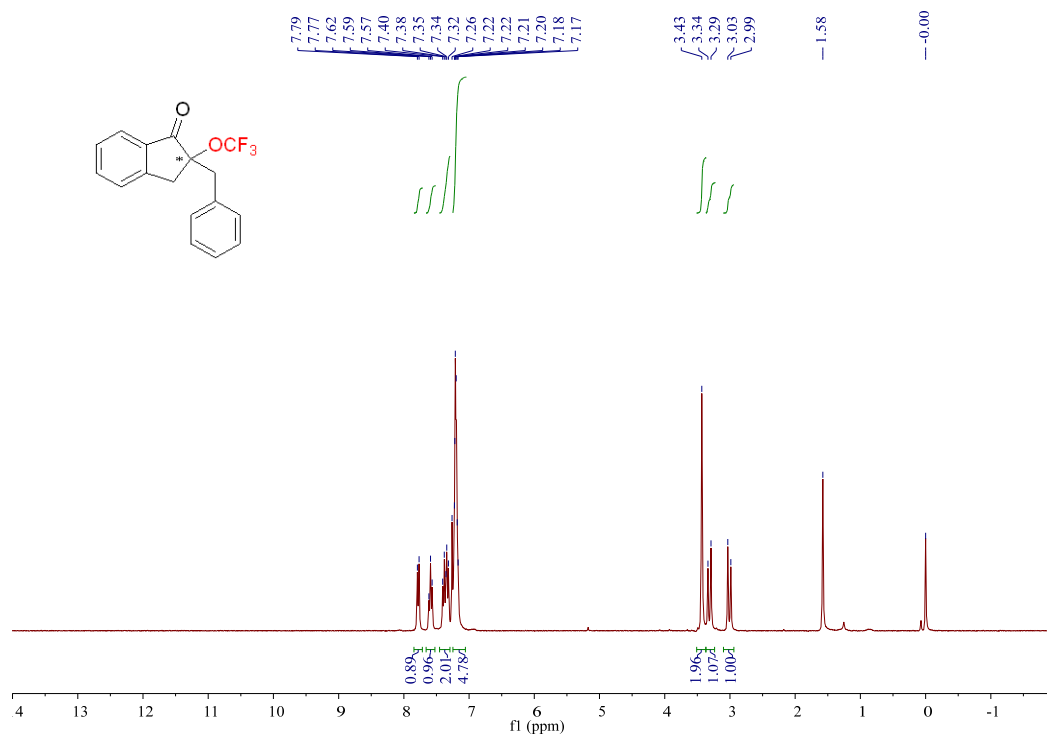


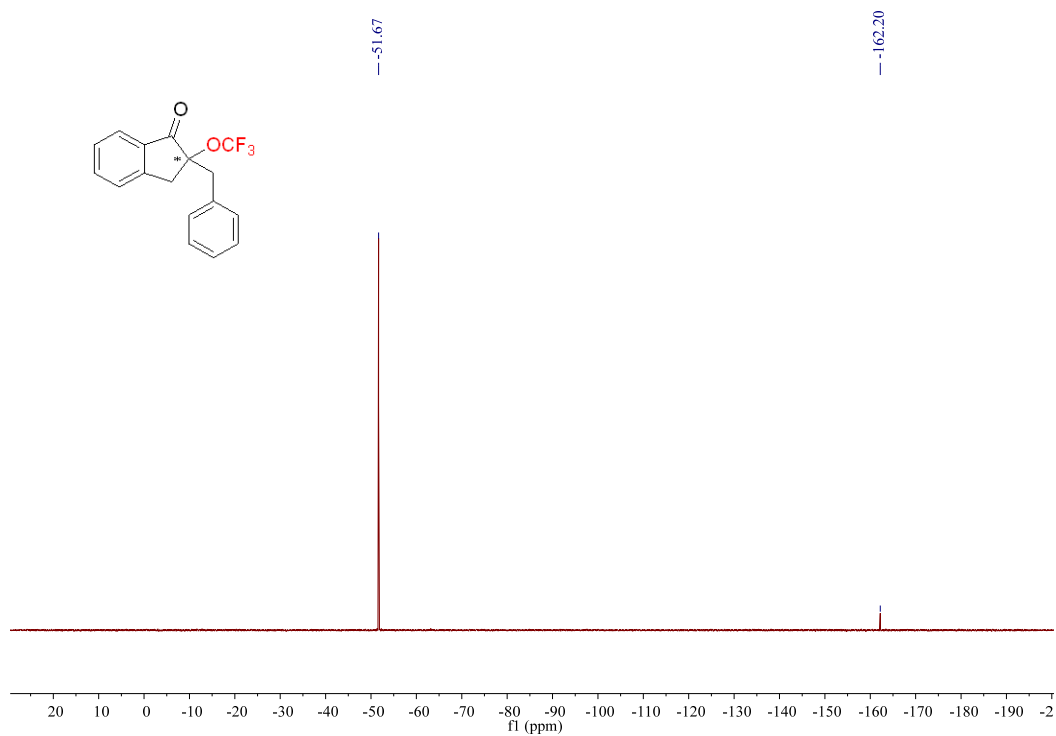
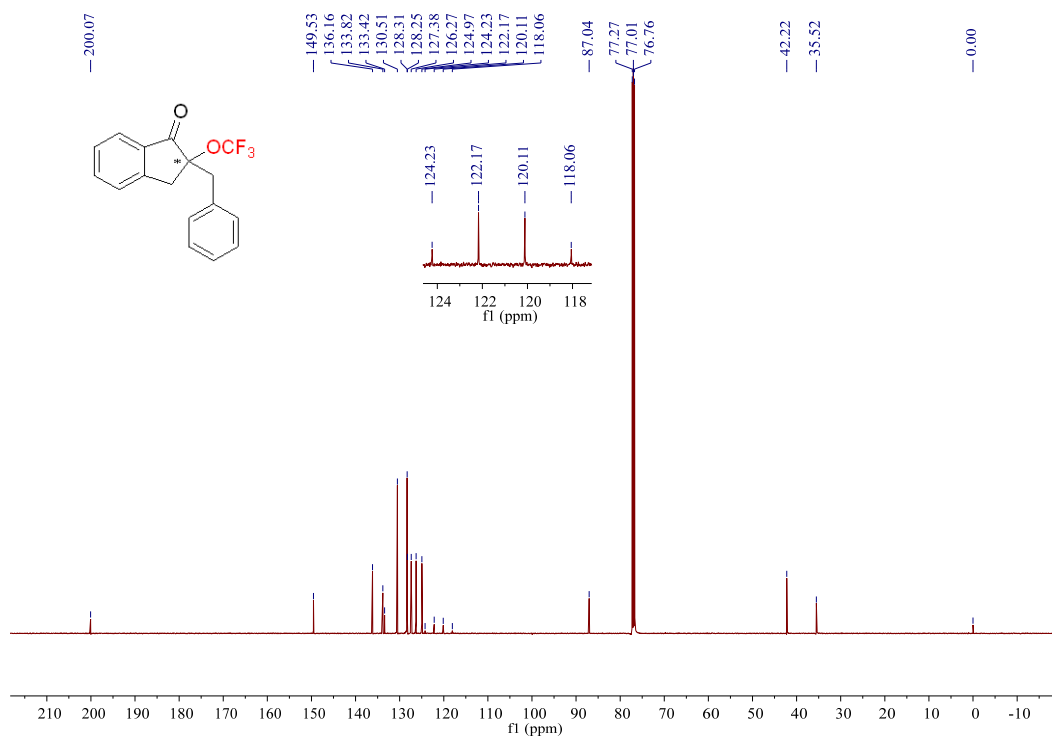
Entry	Cat.	Base	Solvent	Time	Yield (%) ²	Ee (%) ³
1	TBAB	KOH	toluene	15	70	-
2	-	KOH	toluene	24	trace	-
3	CN-10	CsOH·H ₂ O	toluene	15	88	36
4	CN-11	CsOH·H ₂ O	toluene	12	93	26
5	CN-12	CsOH·H ₂ O	toluene	15	16	19
6	QD-4	CsOH·H ₂ O	toluene	15	67	49
7	QN-4	CsOH·H ₂ O	toluene	15	71	-50
8	QD-13	CsOH·H ₂ O	toluene	15	18	17

¹ Reaction conditions: **1a** (0.1mmol, 1.0 equiv.), BnBr **2a** (0.15mmol 1.5 equiv.), base (0.2mmol, 2.0 equiv.) and **cat.** (10.0 mol%) were stirred in anhydrous toluene 5.0 mL at room temperature. ² Isolated yields. ³ Ee was determined by chiral HPLC. CN = Cinchonine, QD = Quinidine, QN = Quinine.

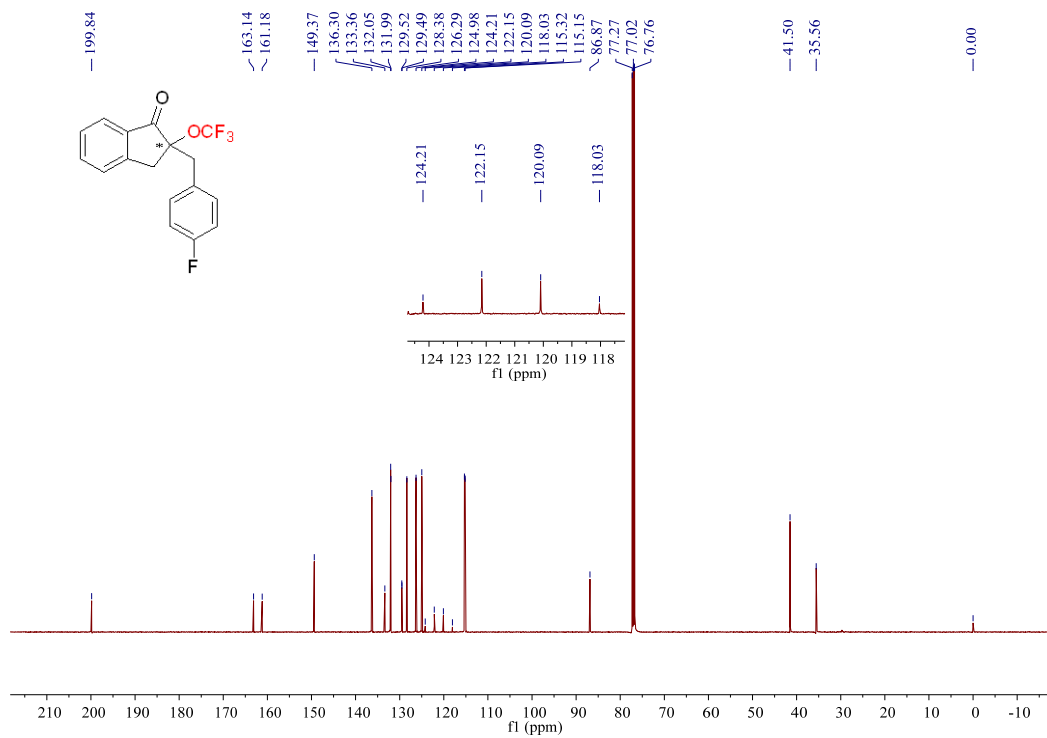
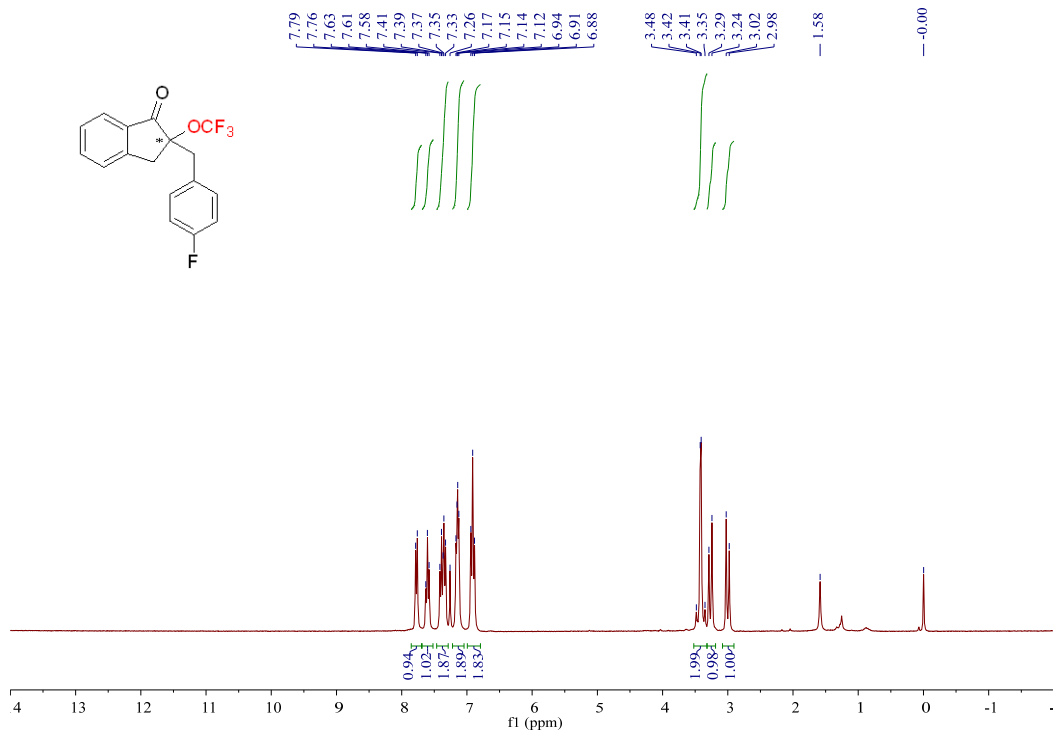
2.¹H, ¹³C and ¹⁹F NMR spectra for desired compounds 3

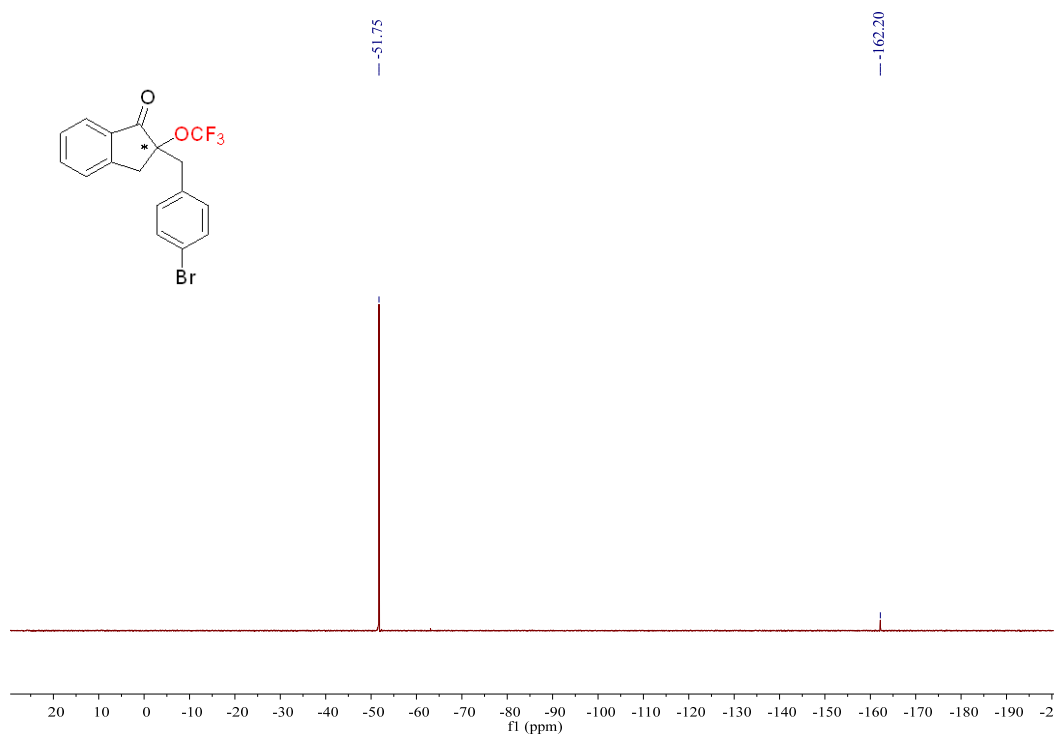
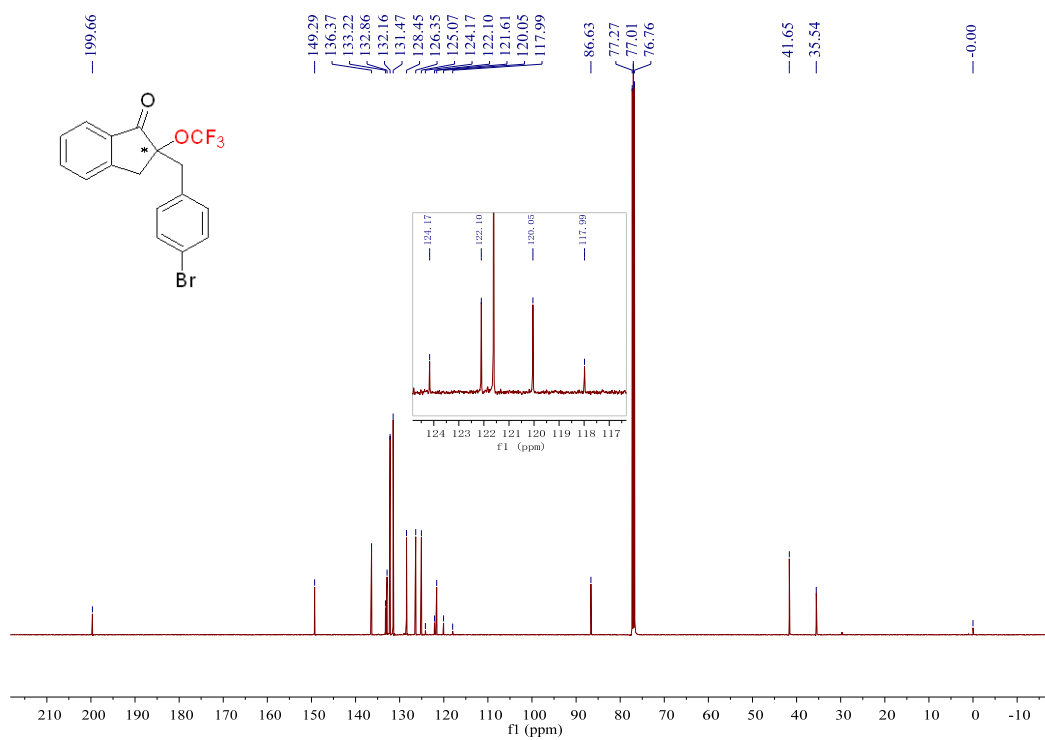
2-Benzyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3aa**).



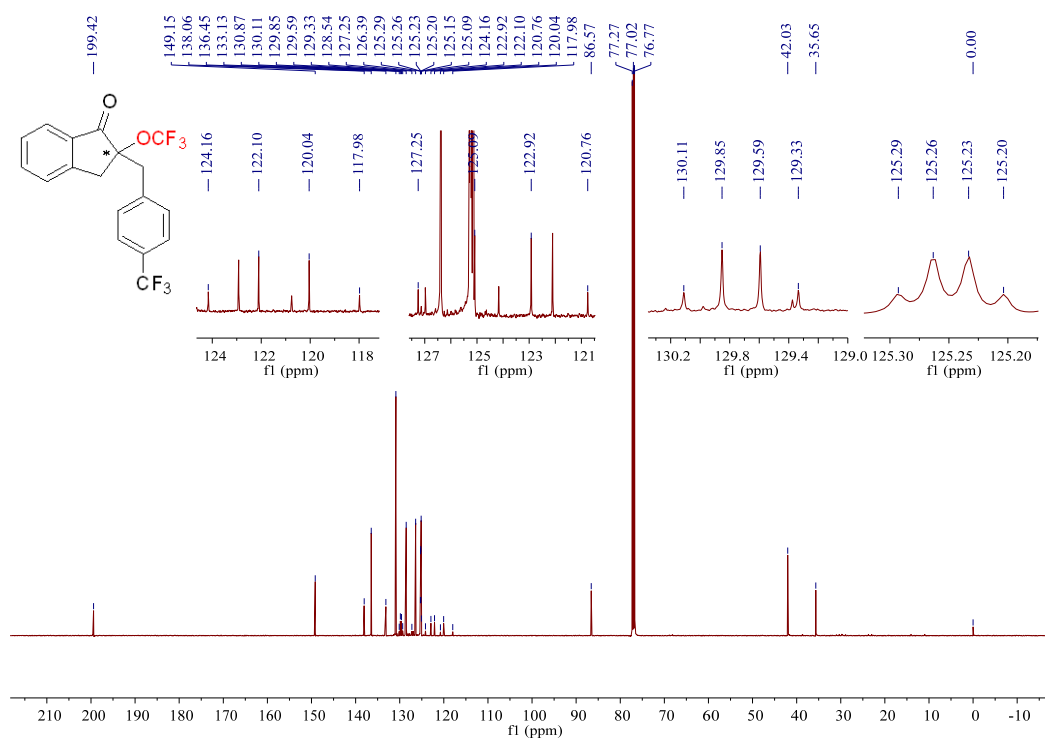
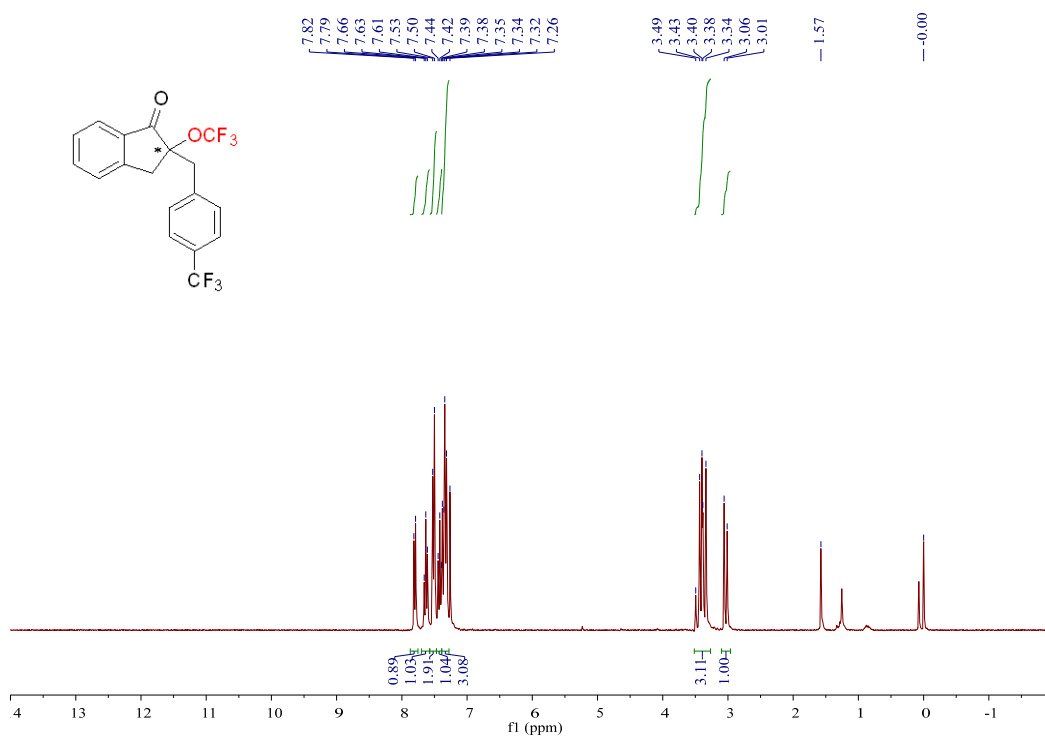


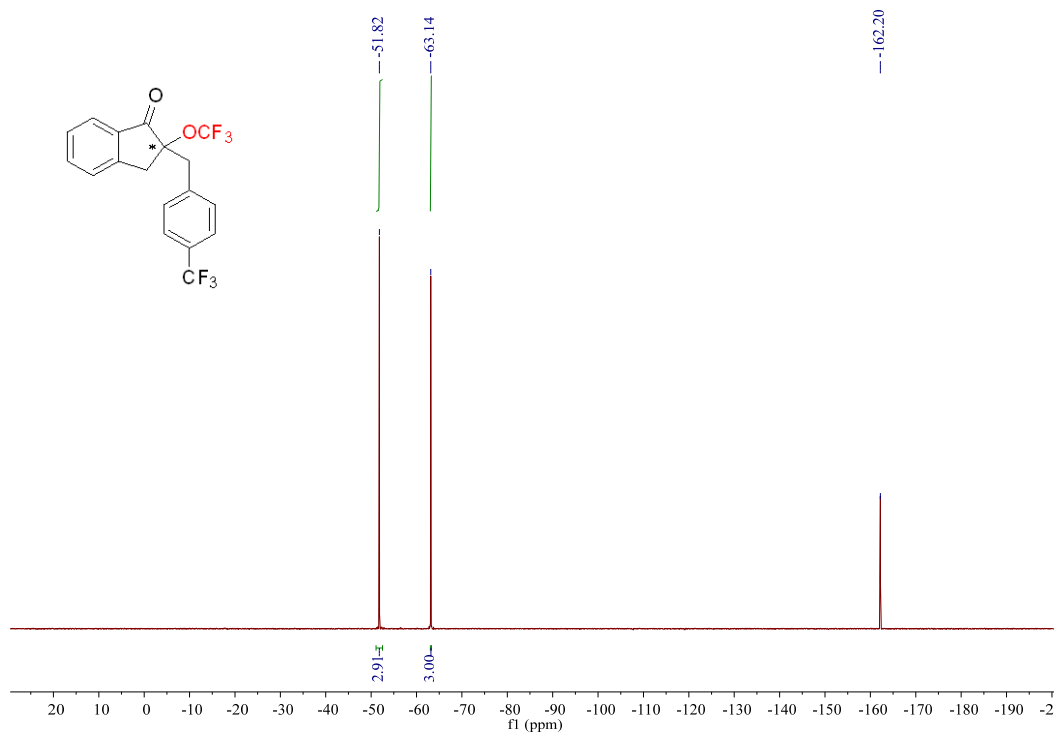
2-(4-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3ab).



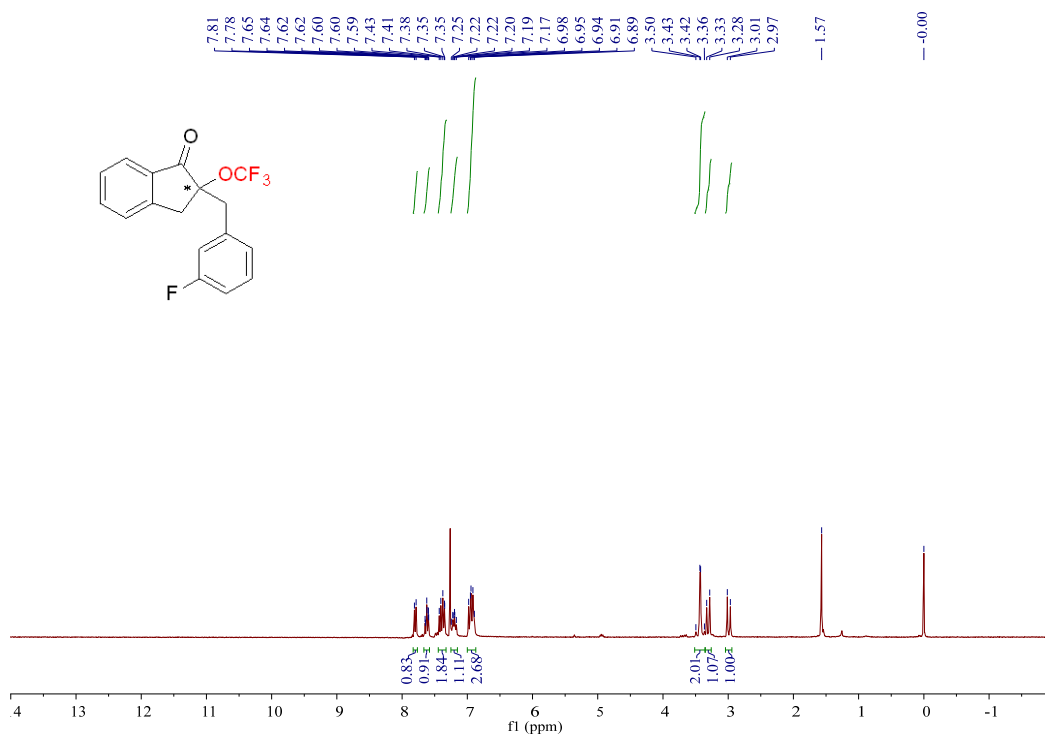


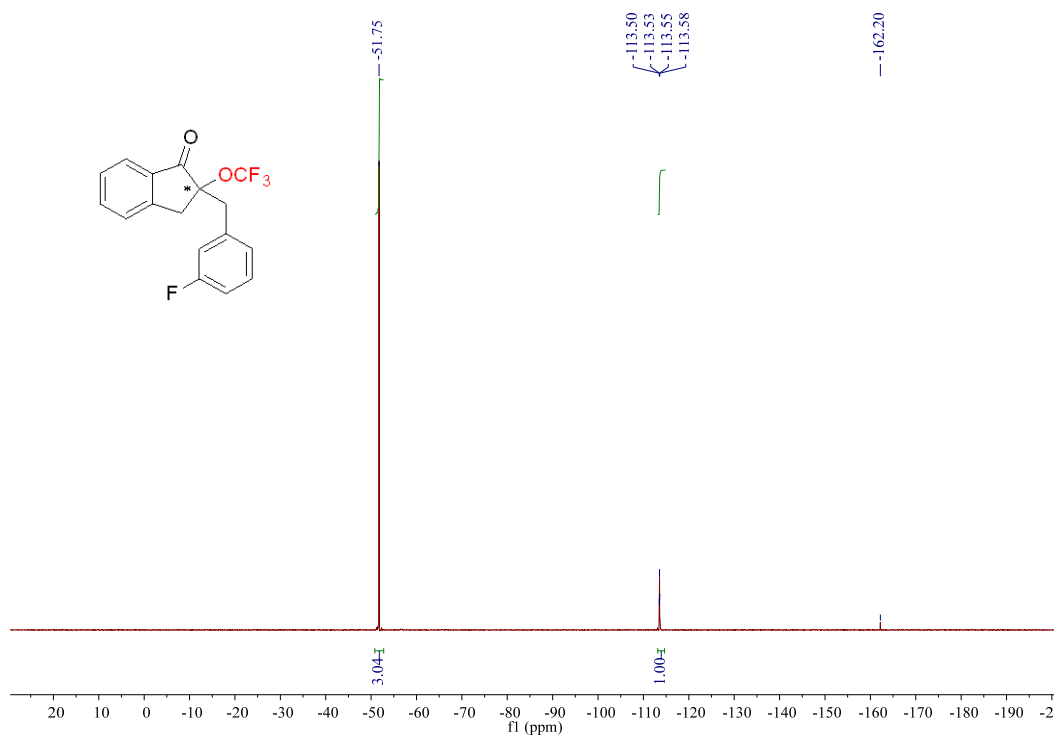
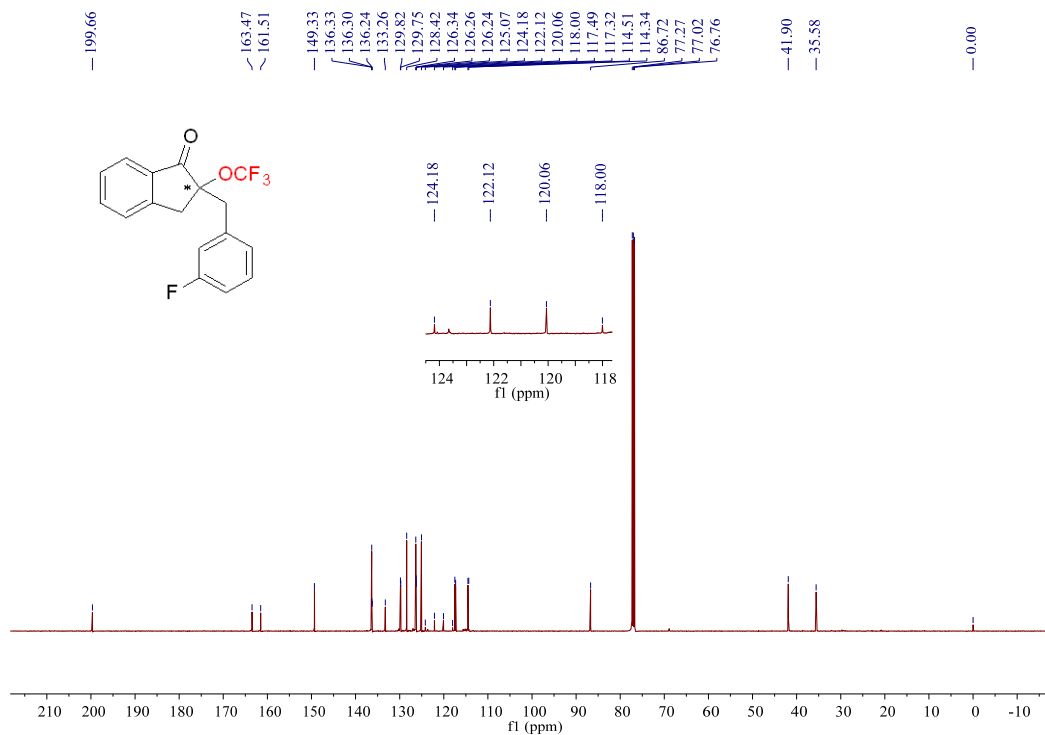
2-(Trifluoromethoxy)-2-(4-(trifluoromethyl)benzyl)-2,3-dihydro-1H-inden-1-one (**3ad**).



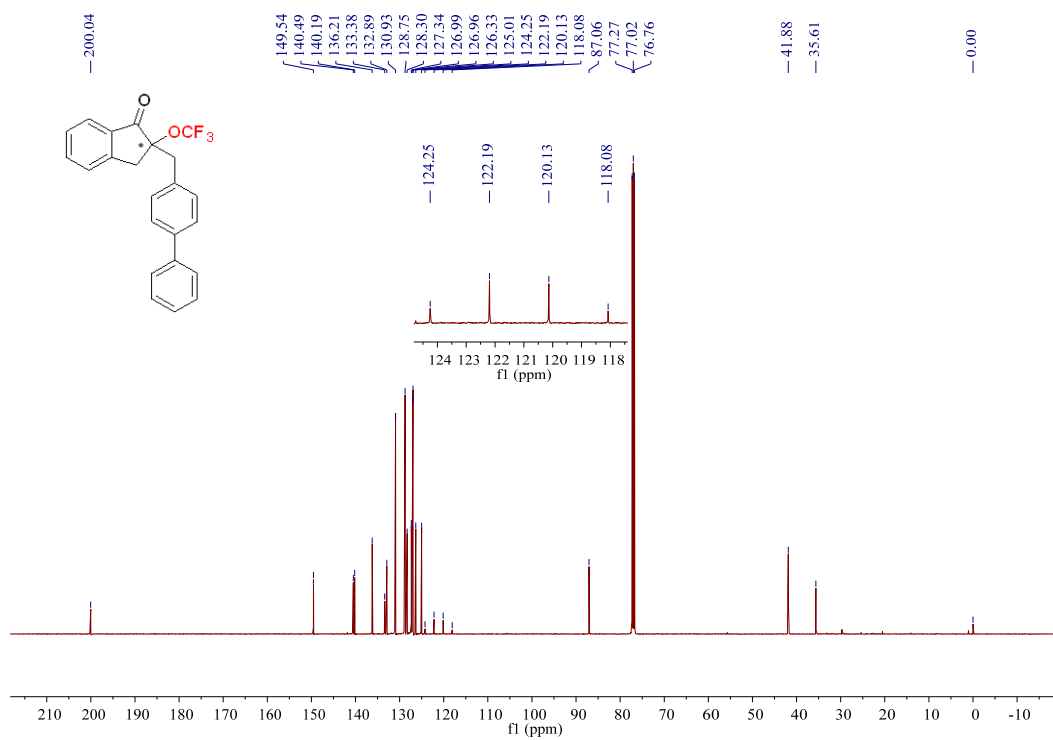
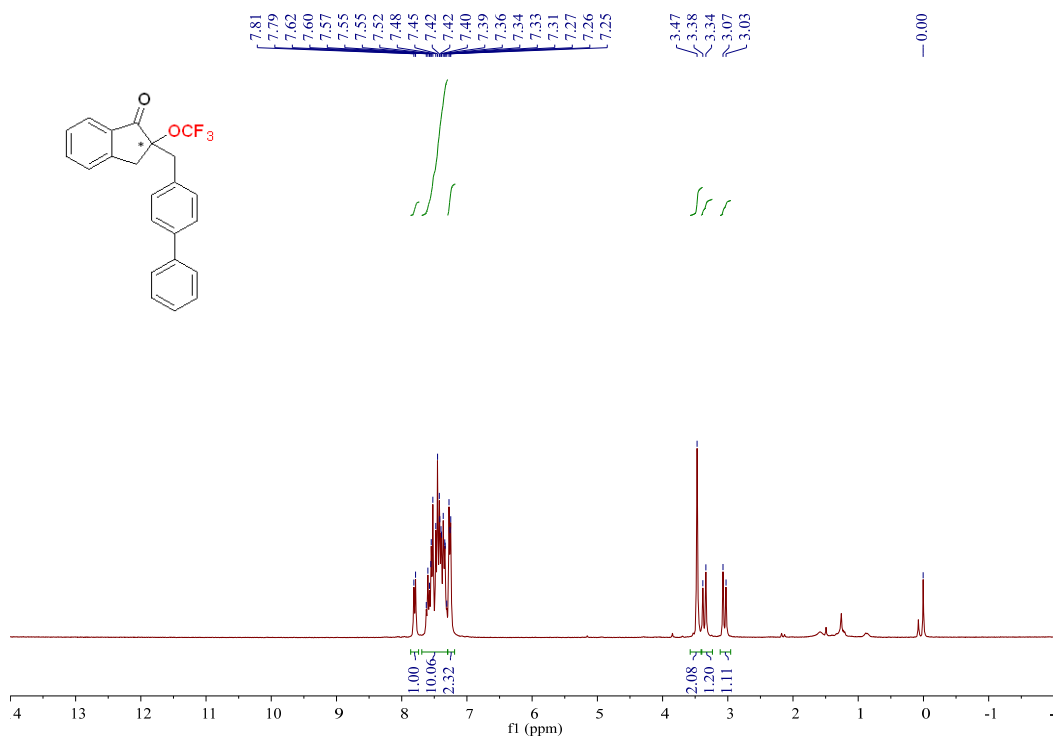


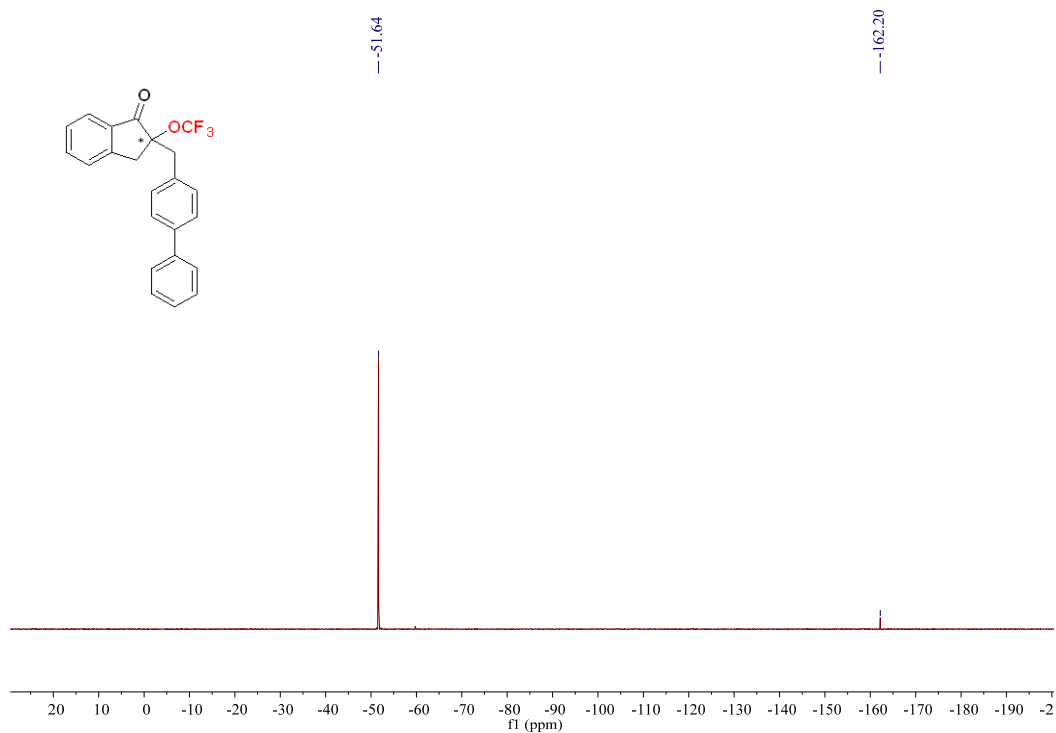
2-(3-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3ae).



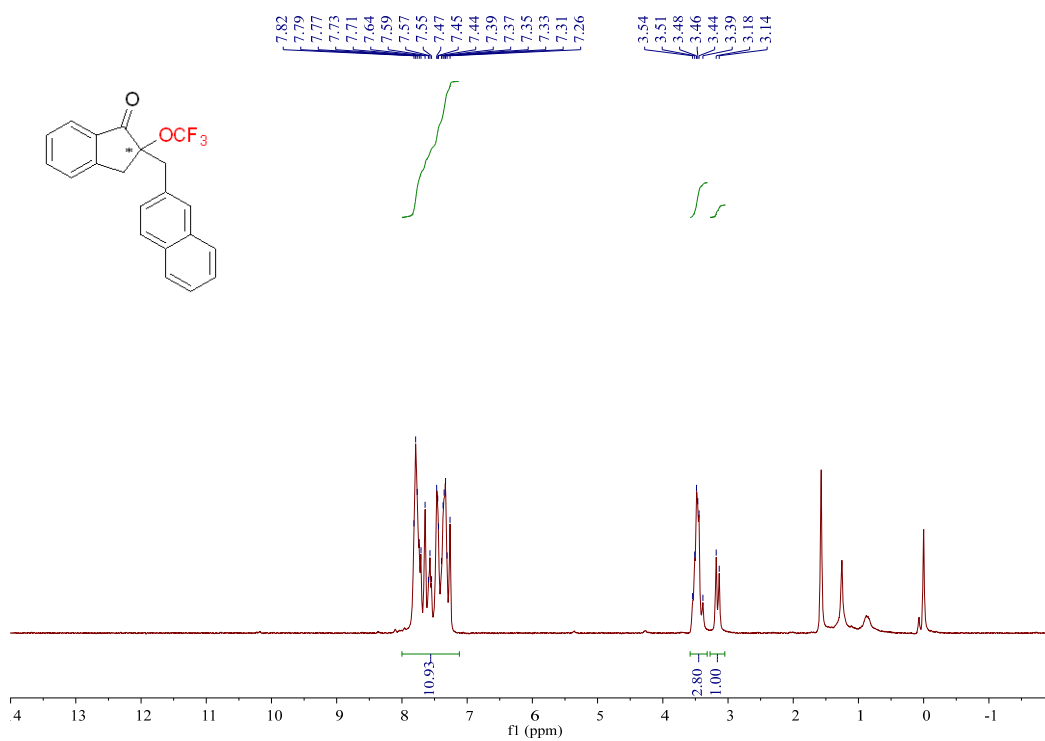


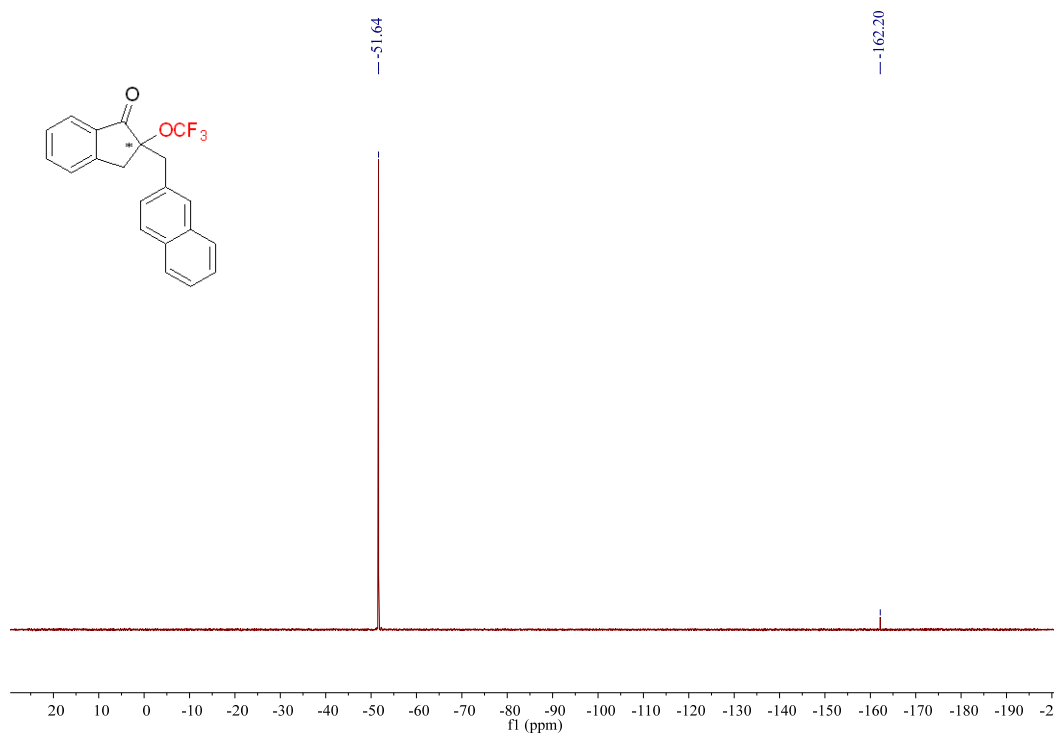
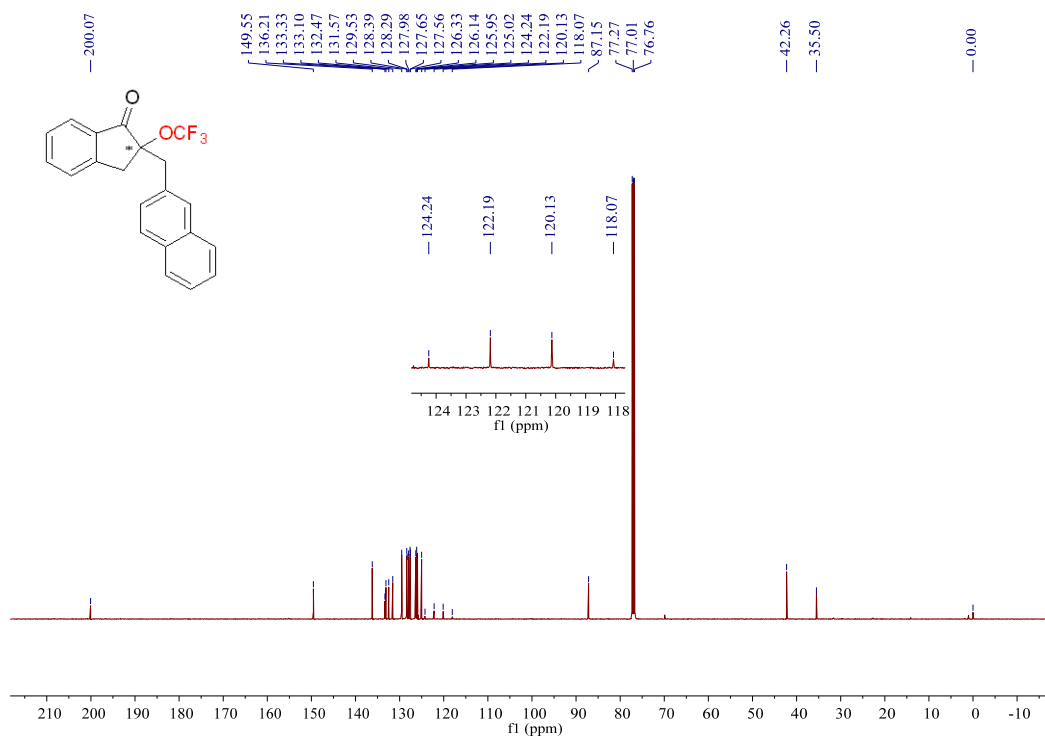
2-([1,1'-Biphenyl]-4-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3af**).



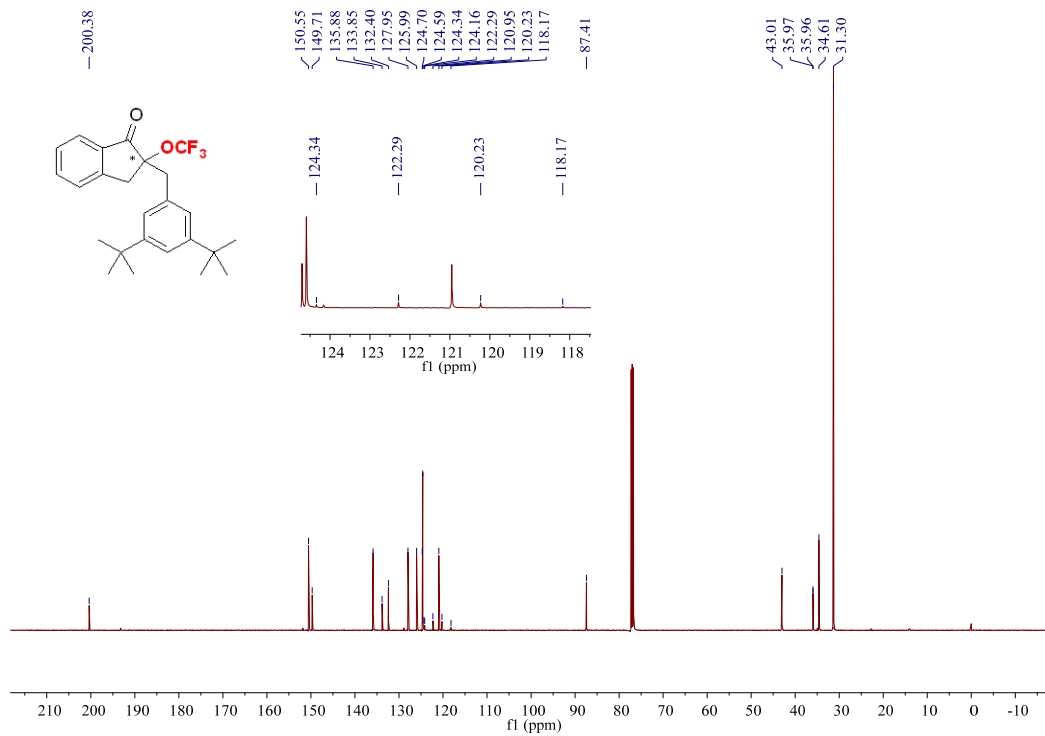
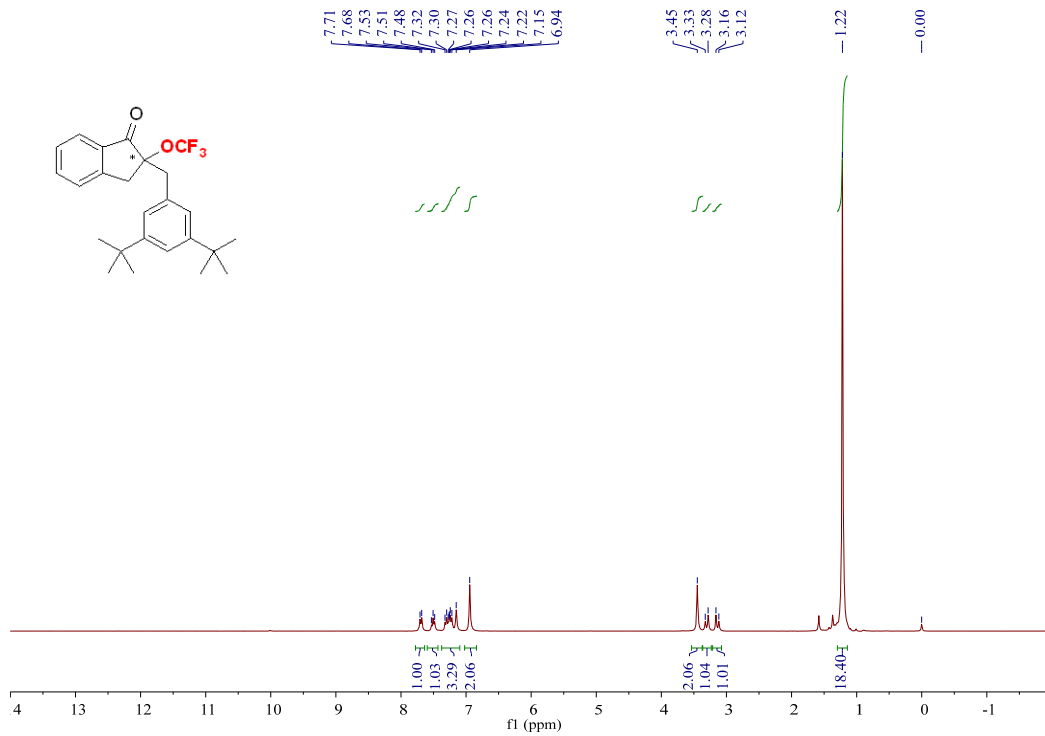


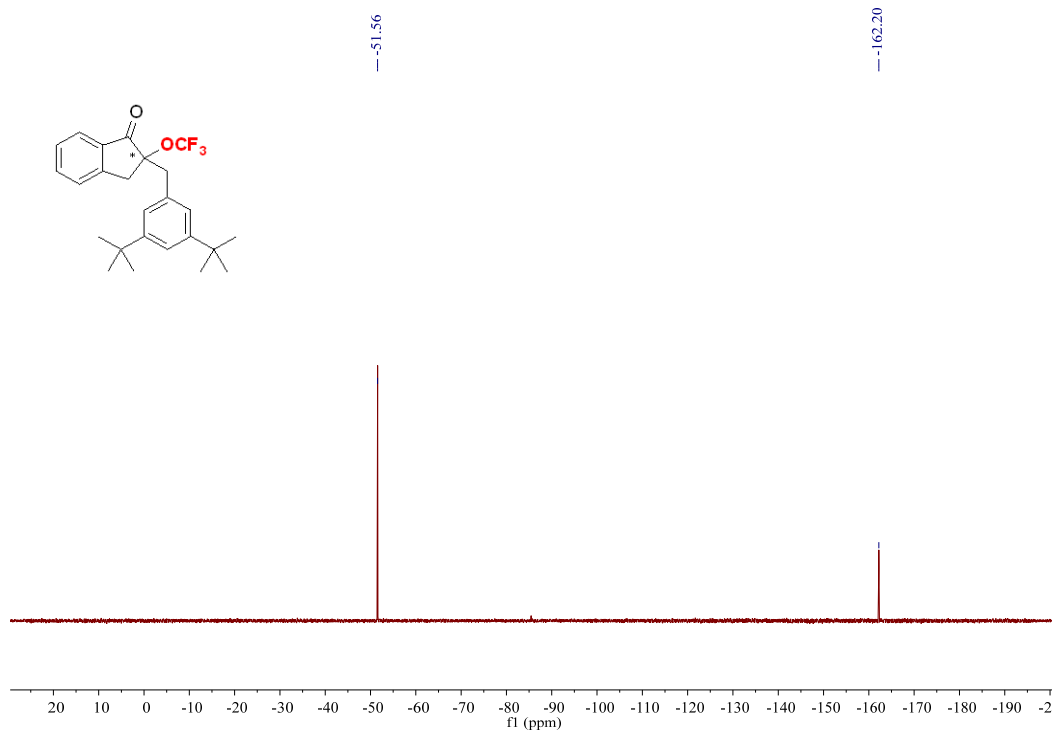
2-(Naphthalen-2-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3ag**).



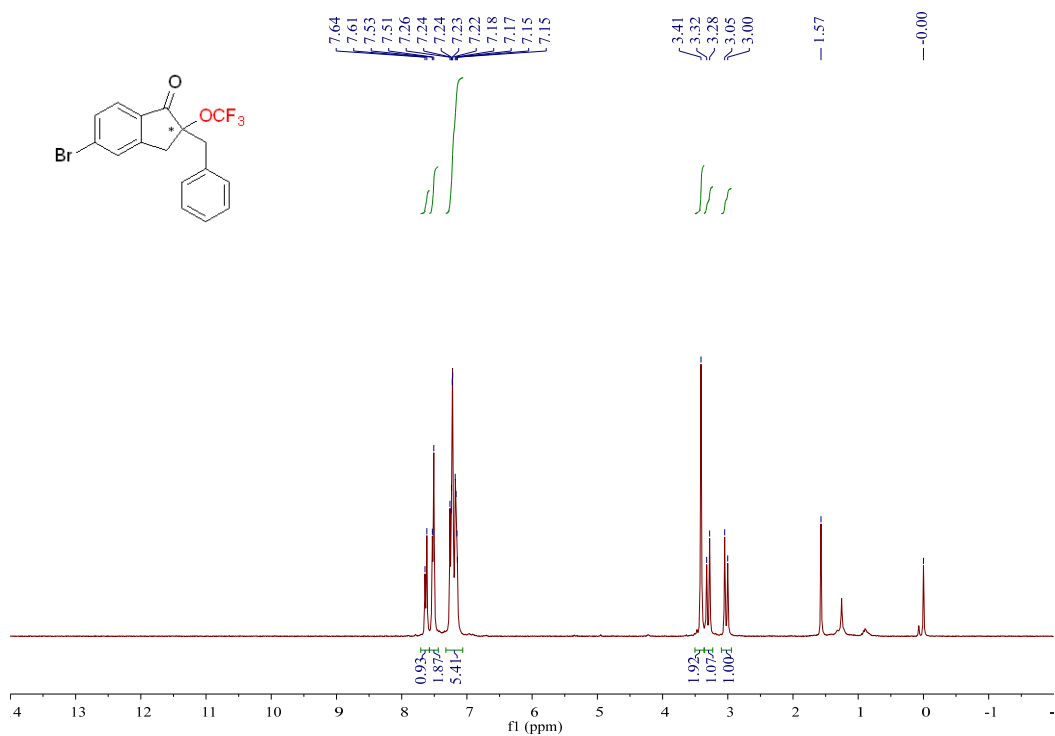


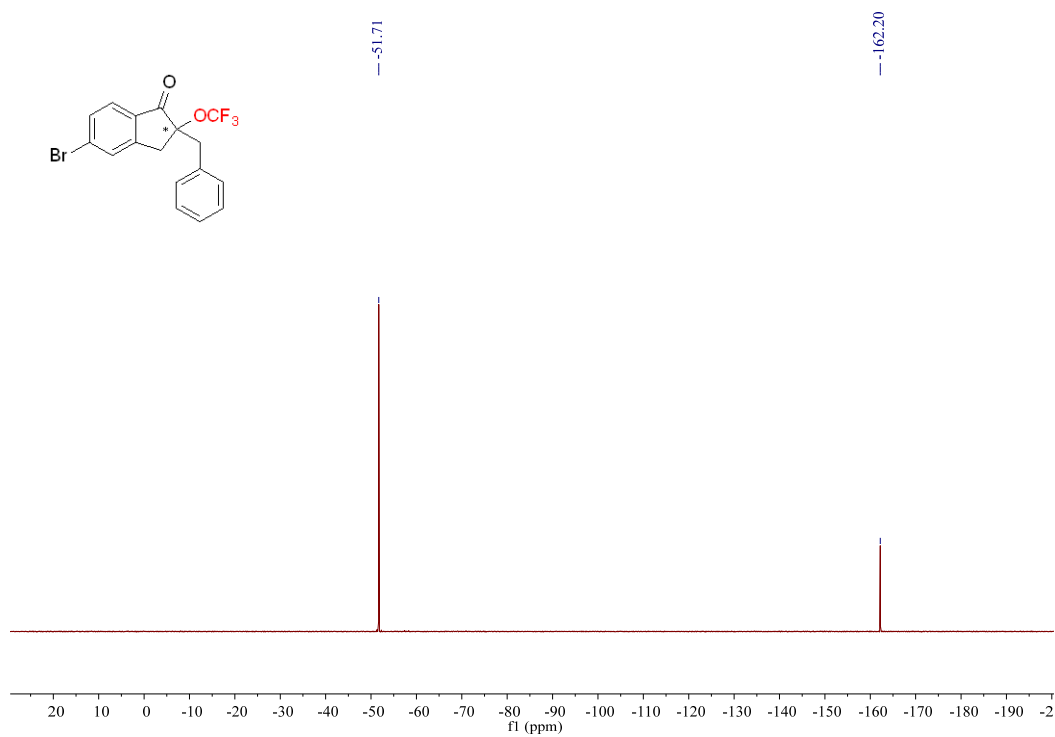
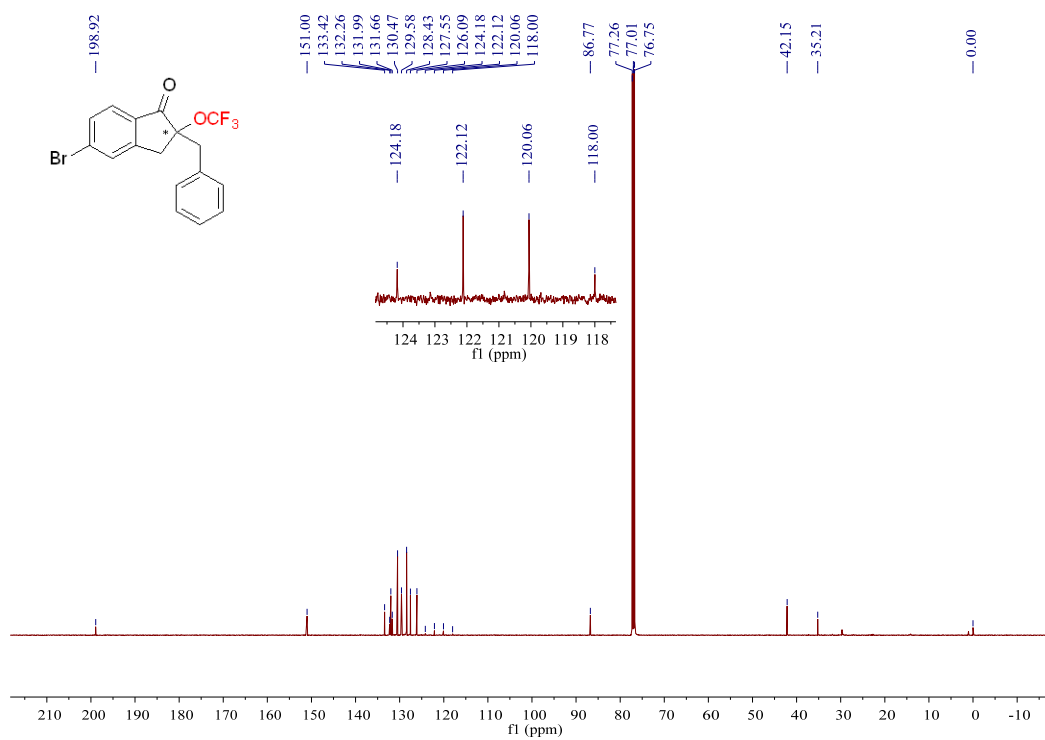
2-(3,5-di-tert-butylbenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3ah).



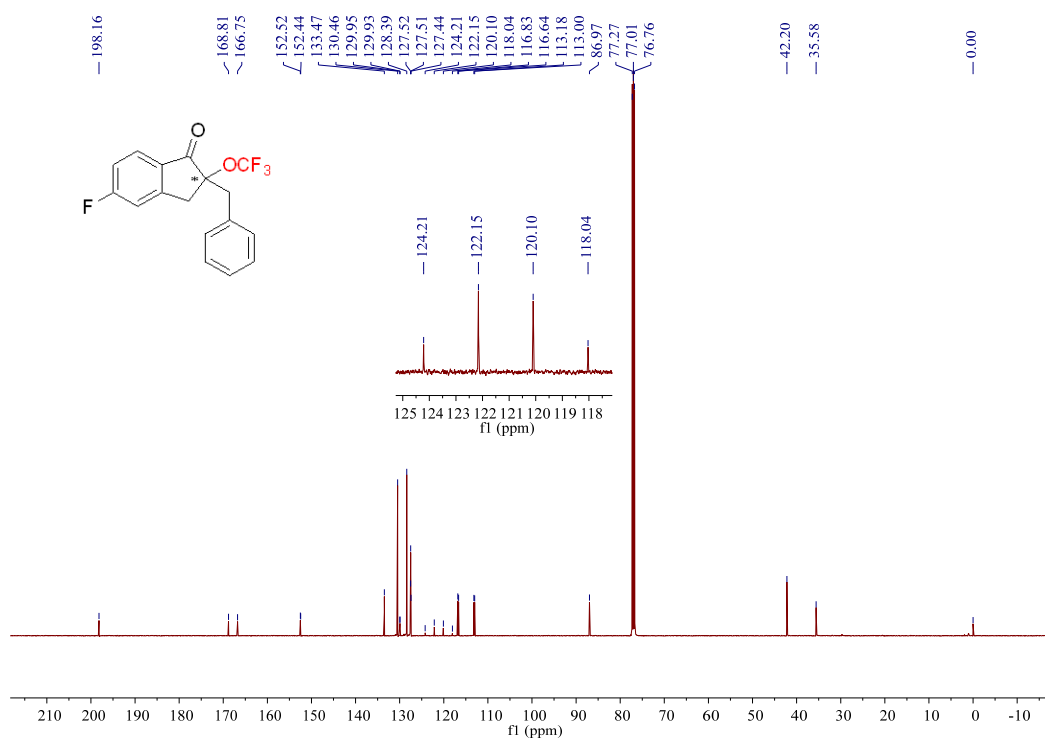
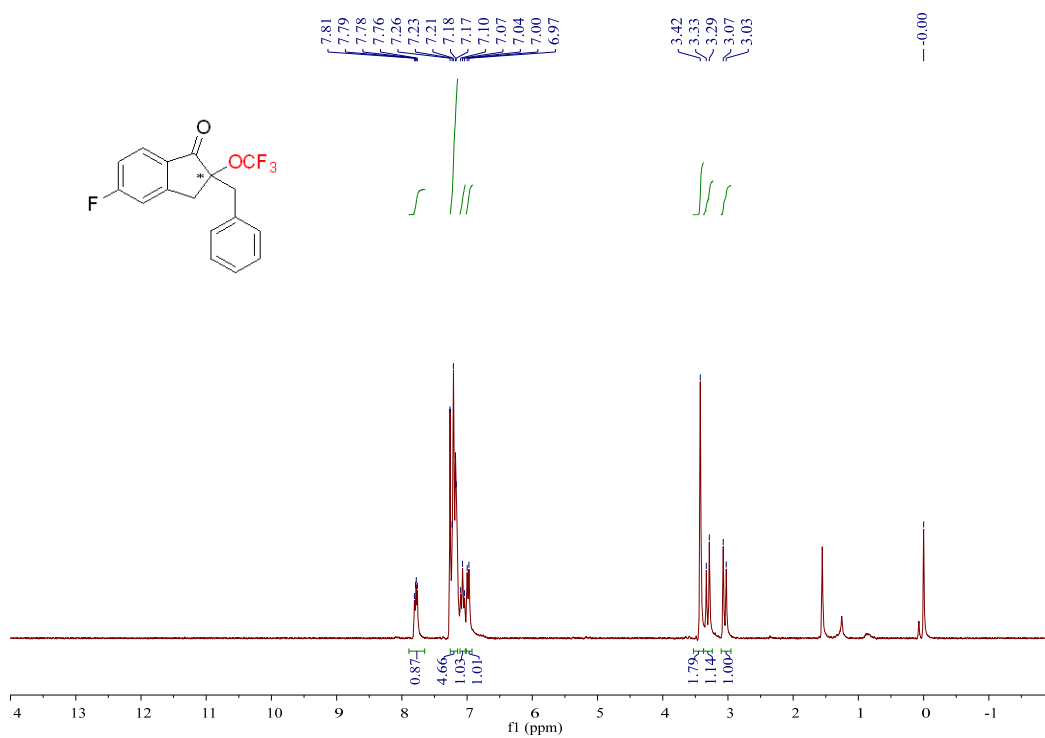


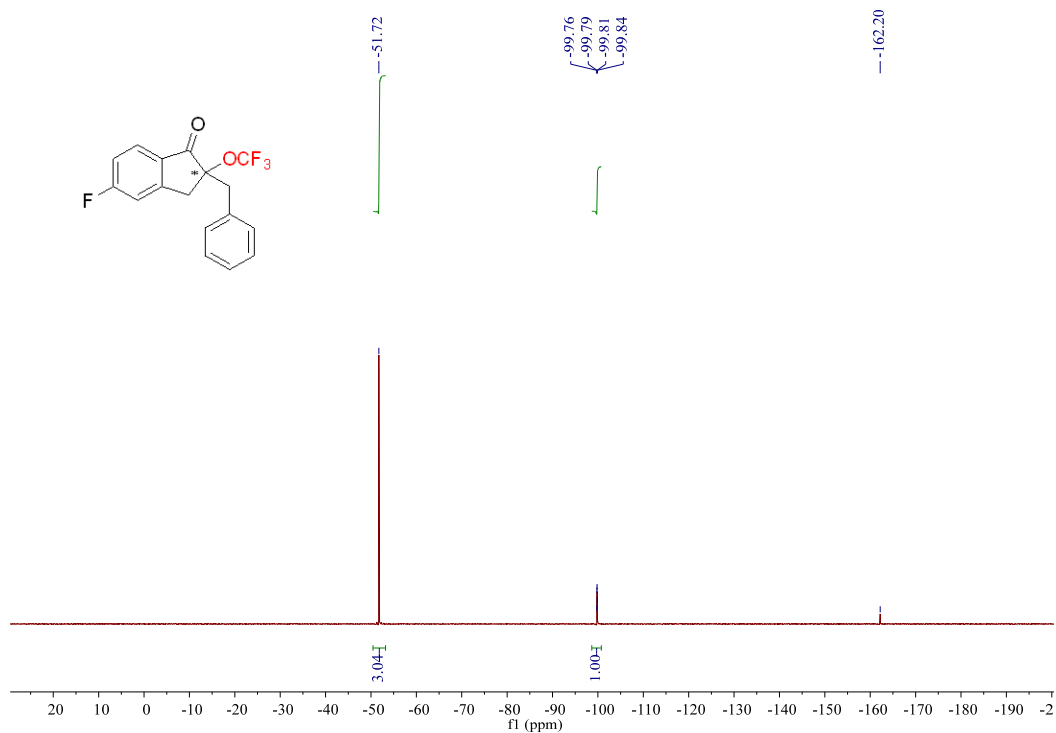
2-Benzyl-5-bromo-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3ba).



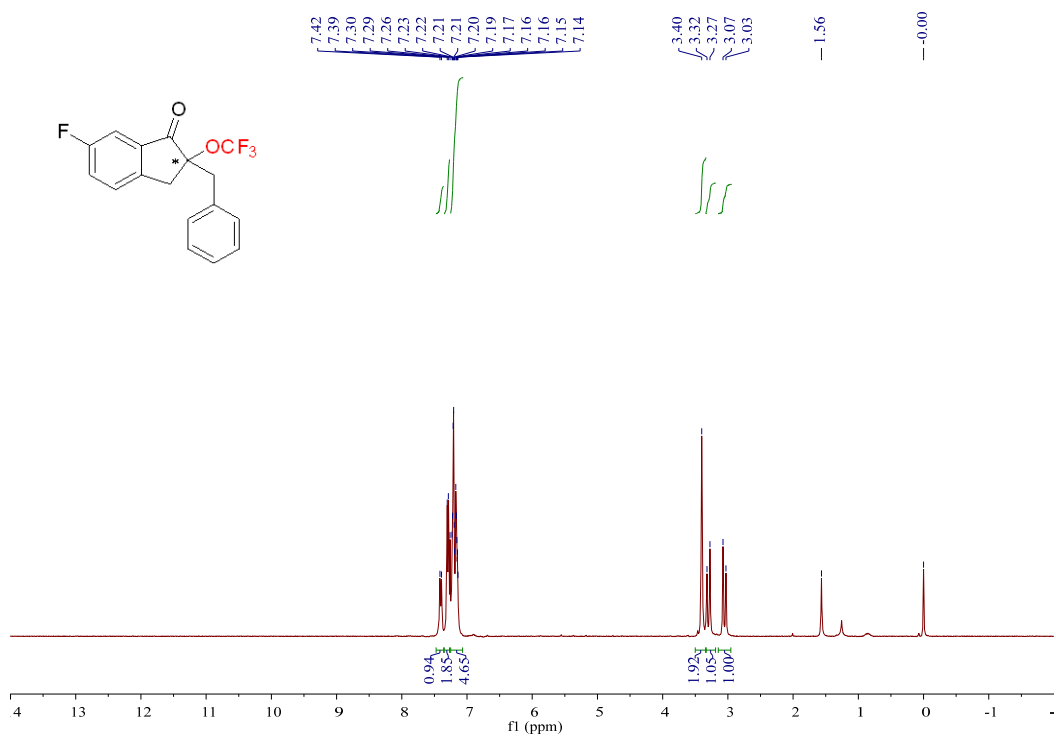


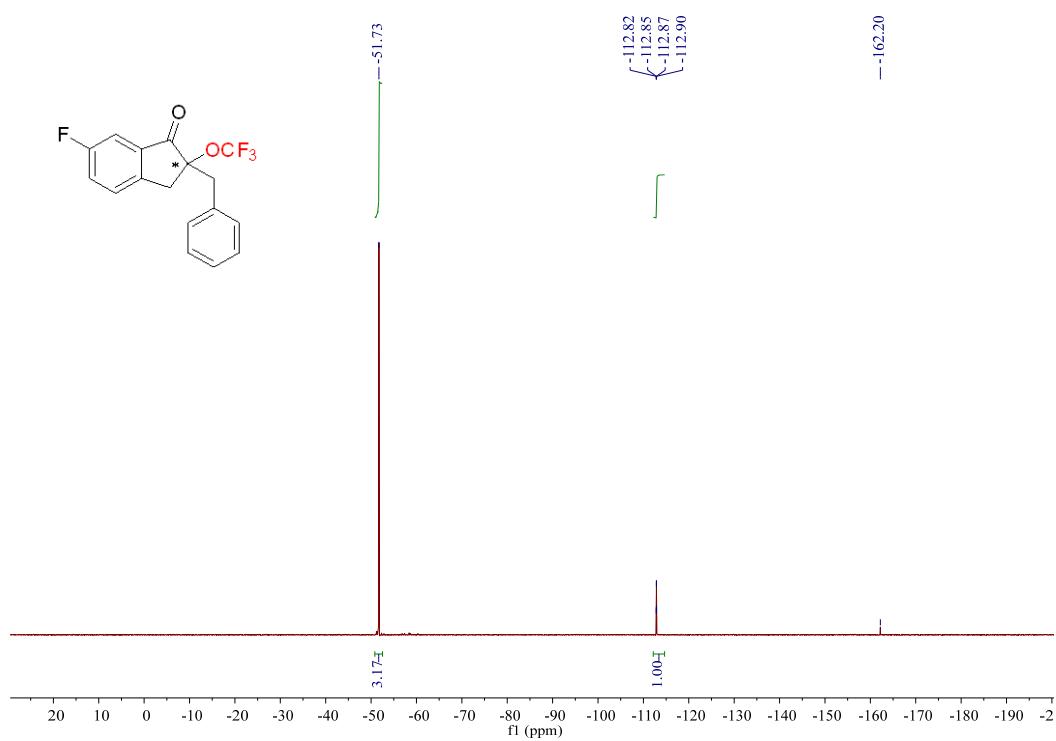
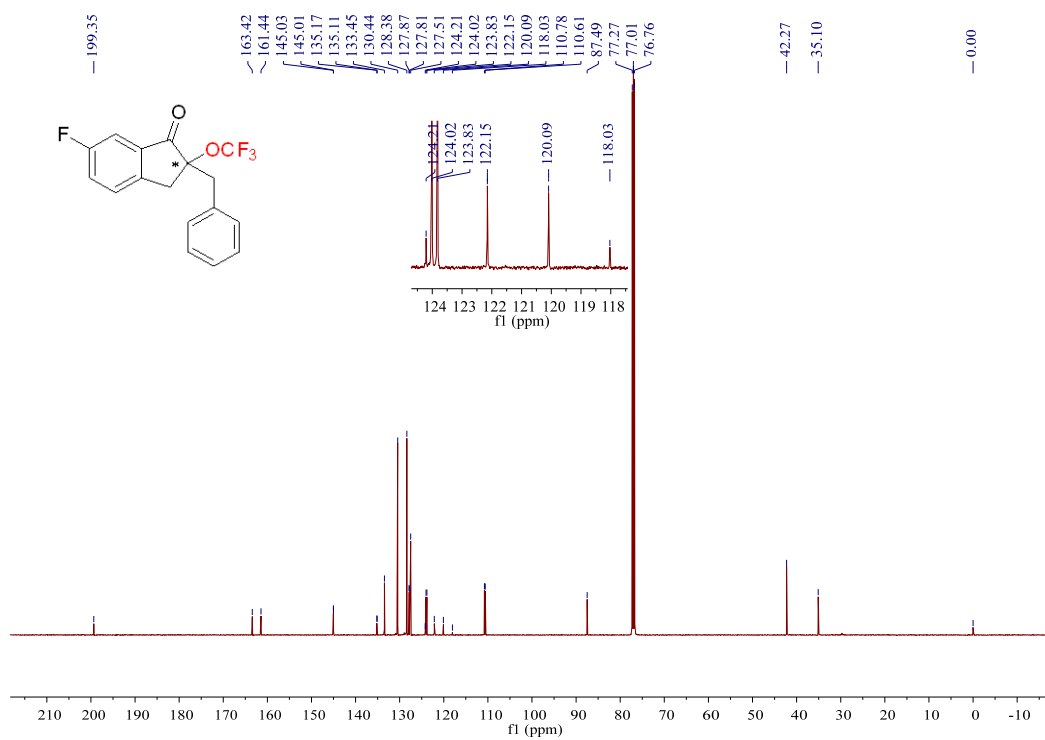
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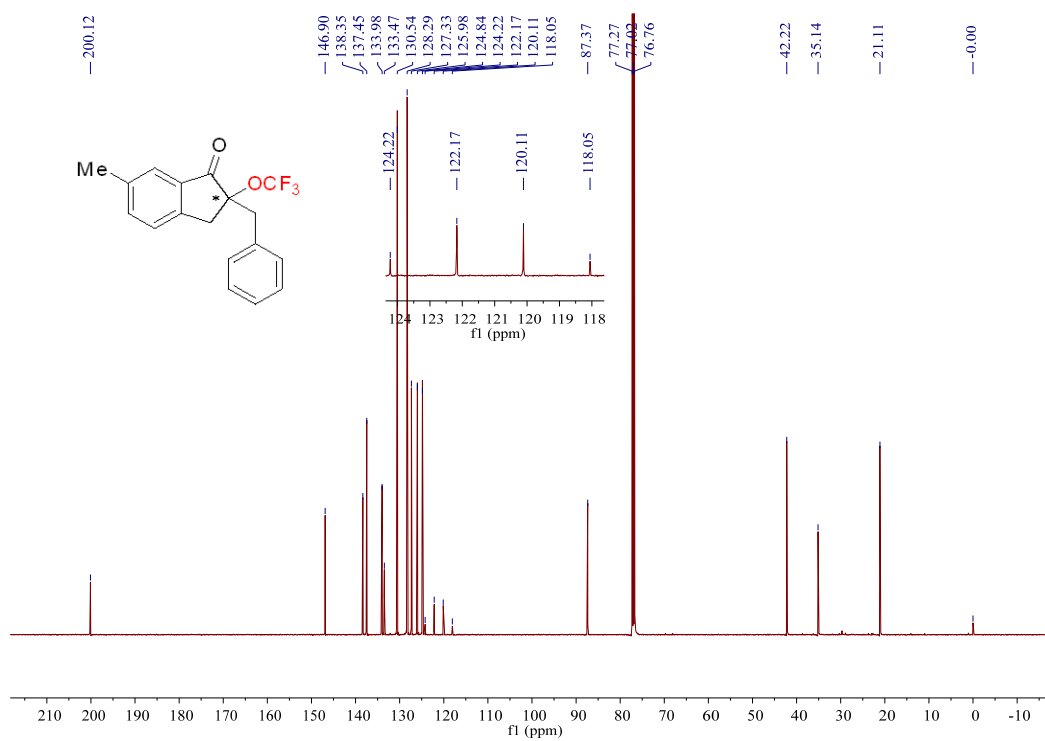
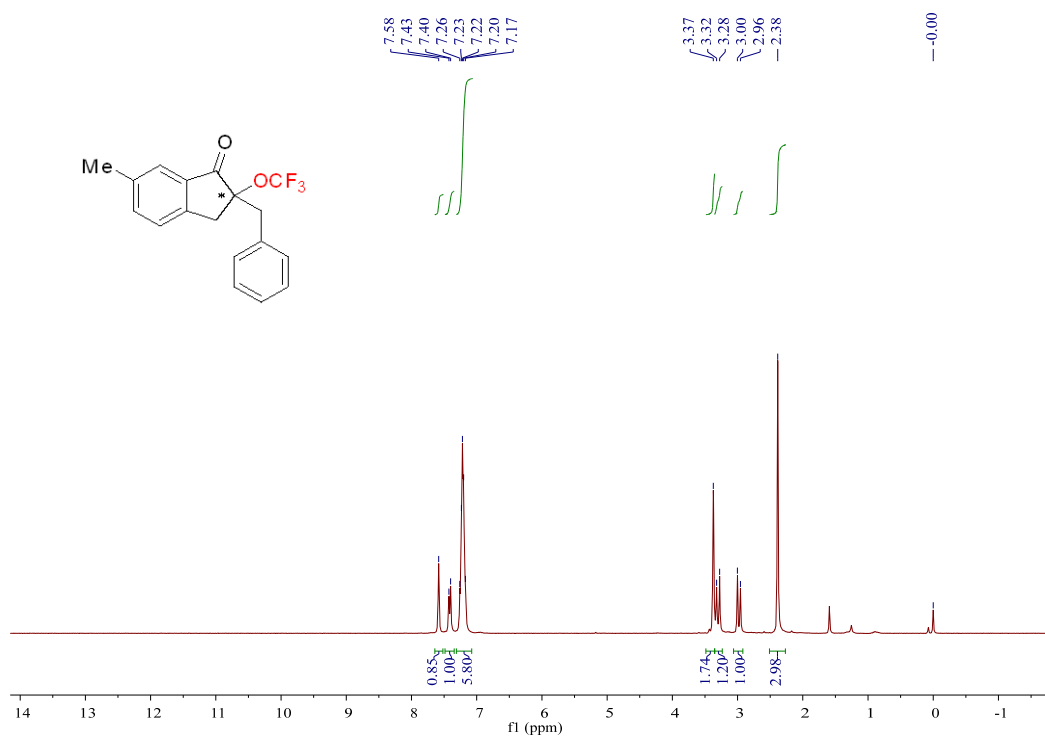


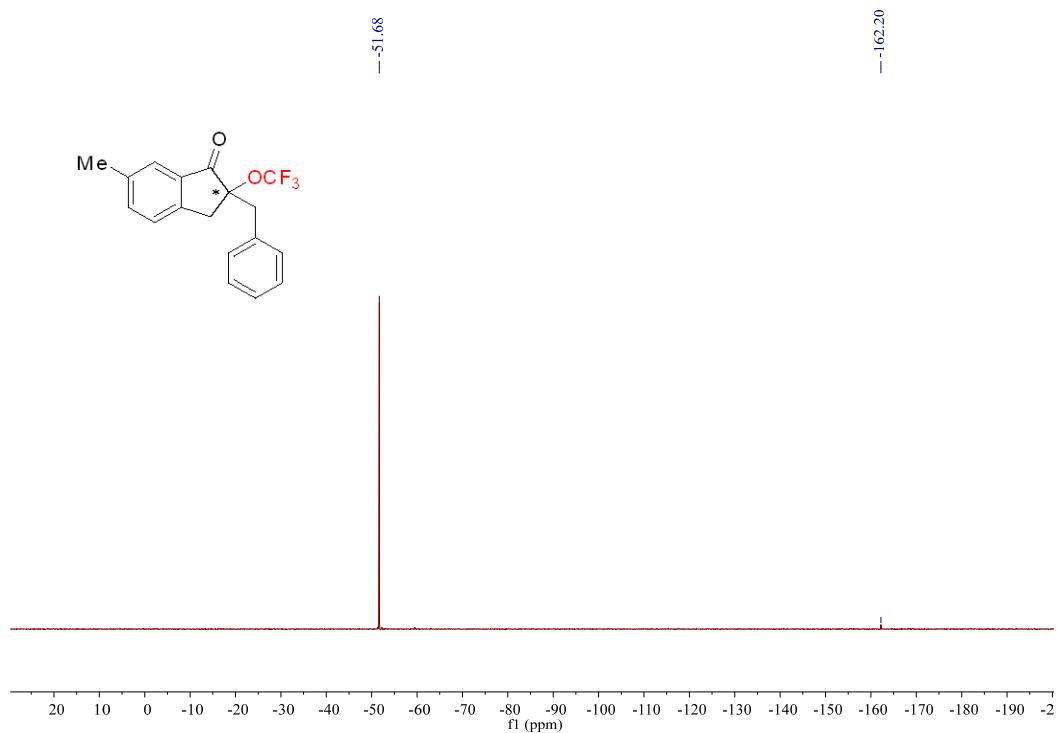
2-Benzyl-6-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3da).



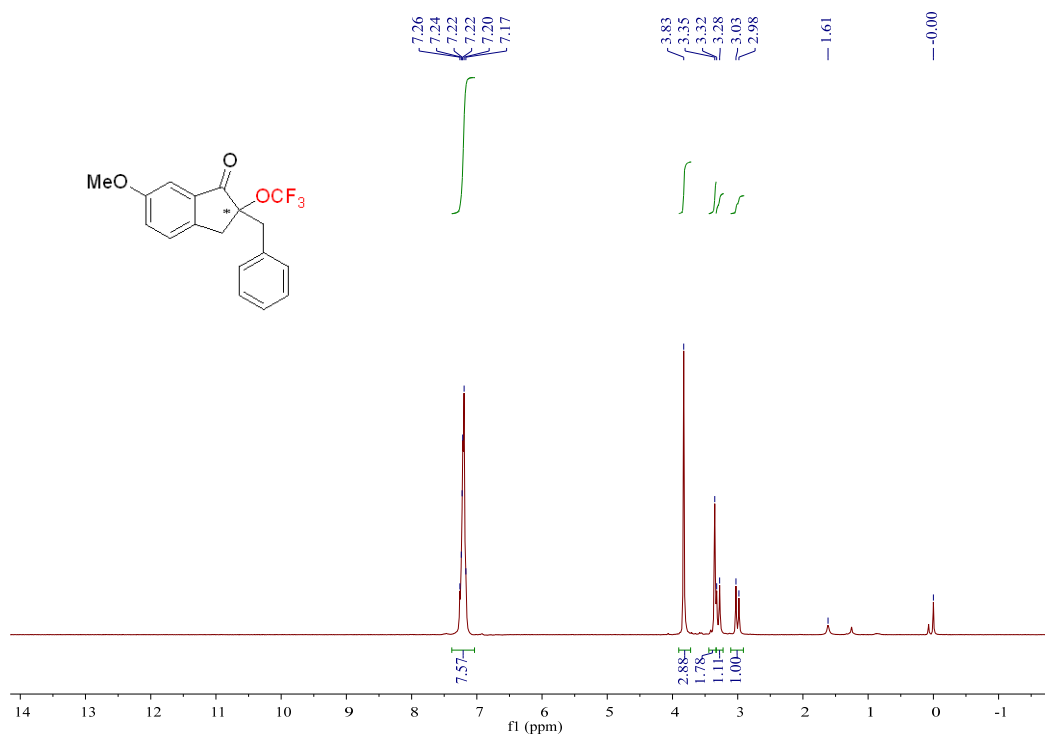


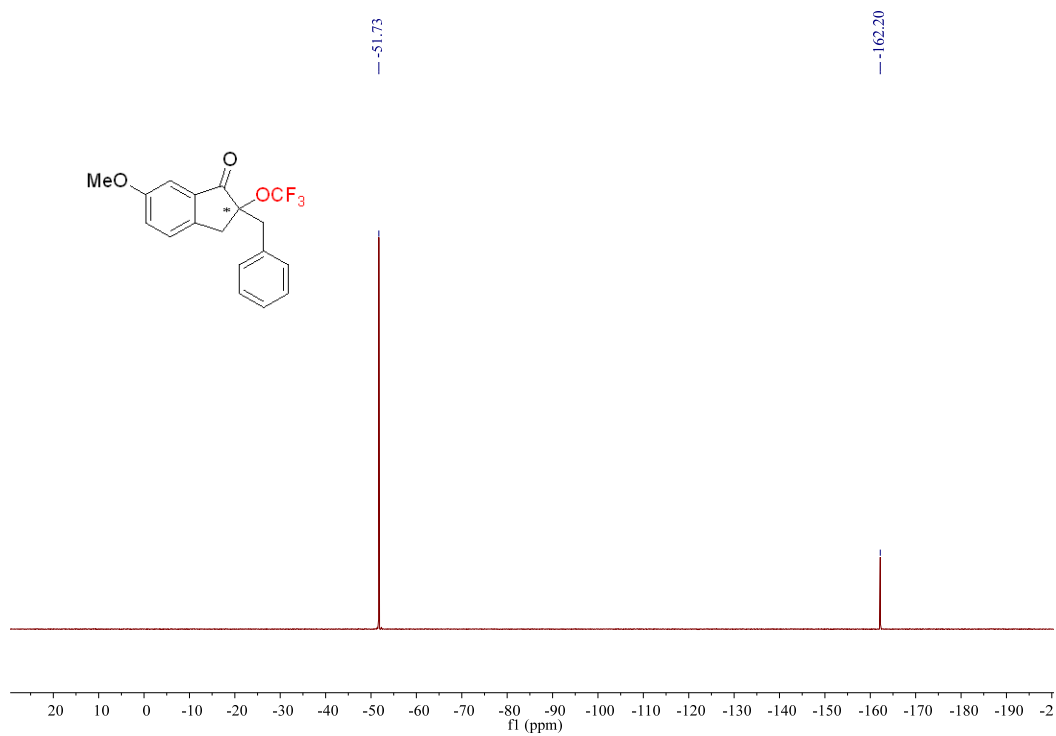
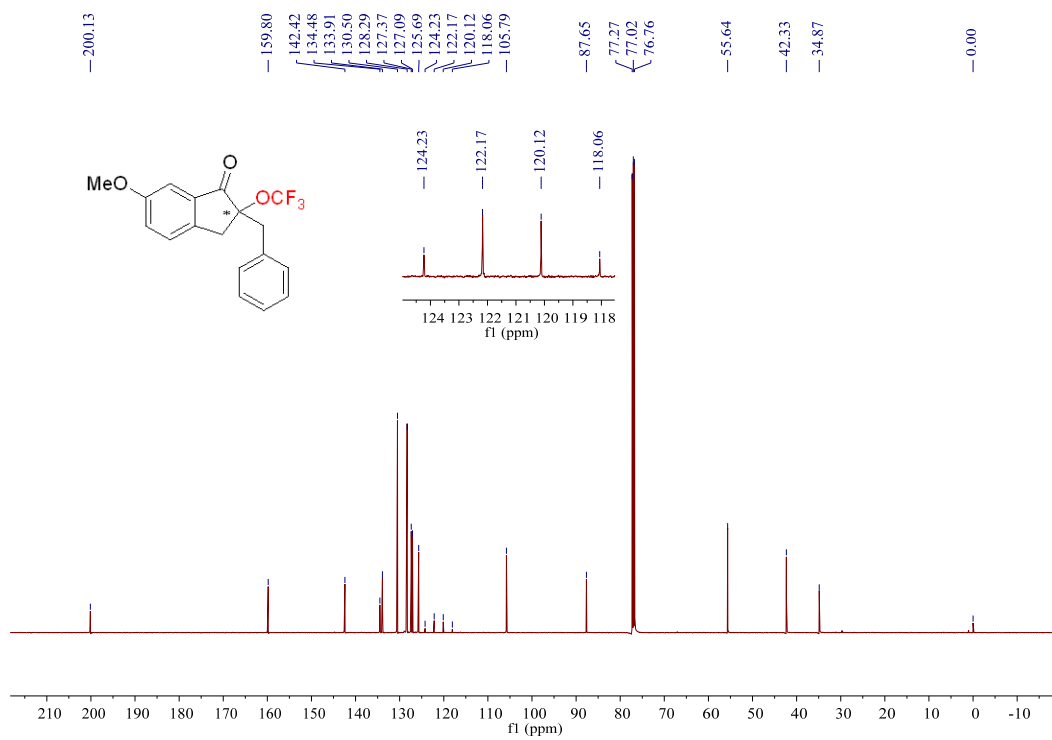
2-Benzyl-6-methyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3ea**).



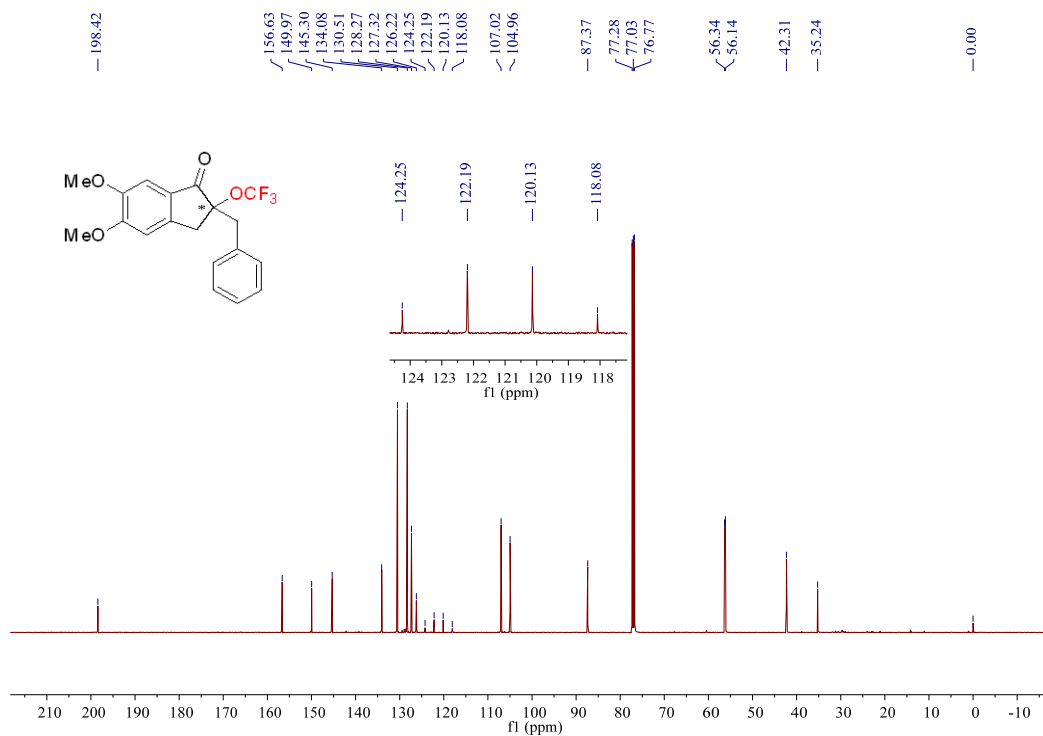
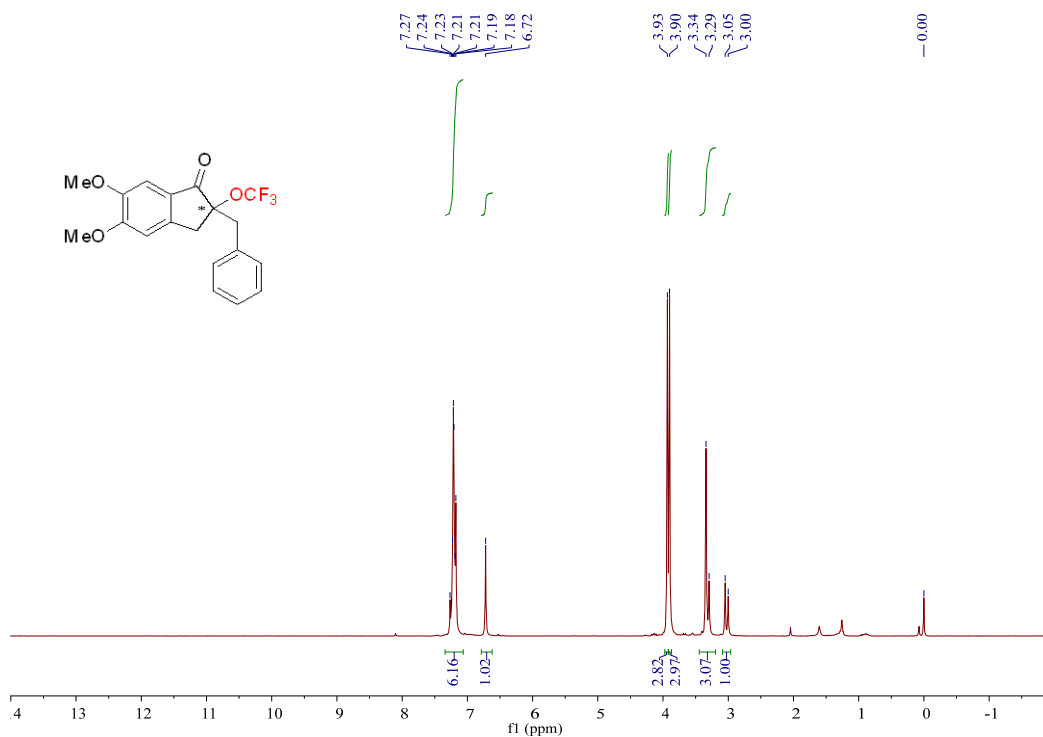


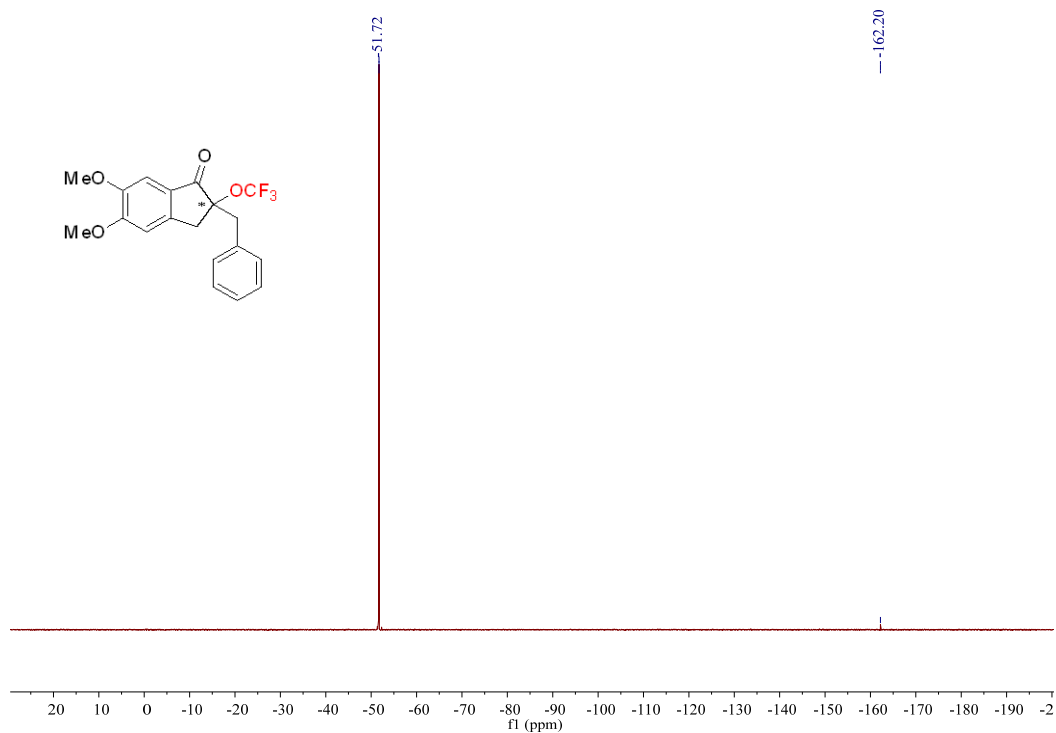
2-Benzyl-6-methoxy-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (3fa).



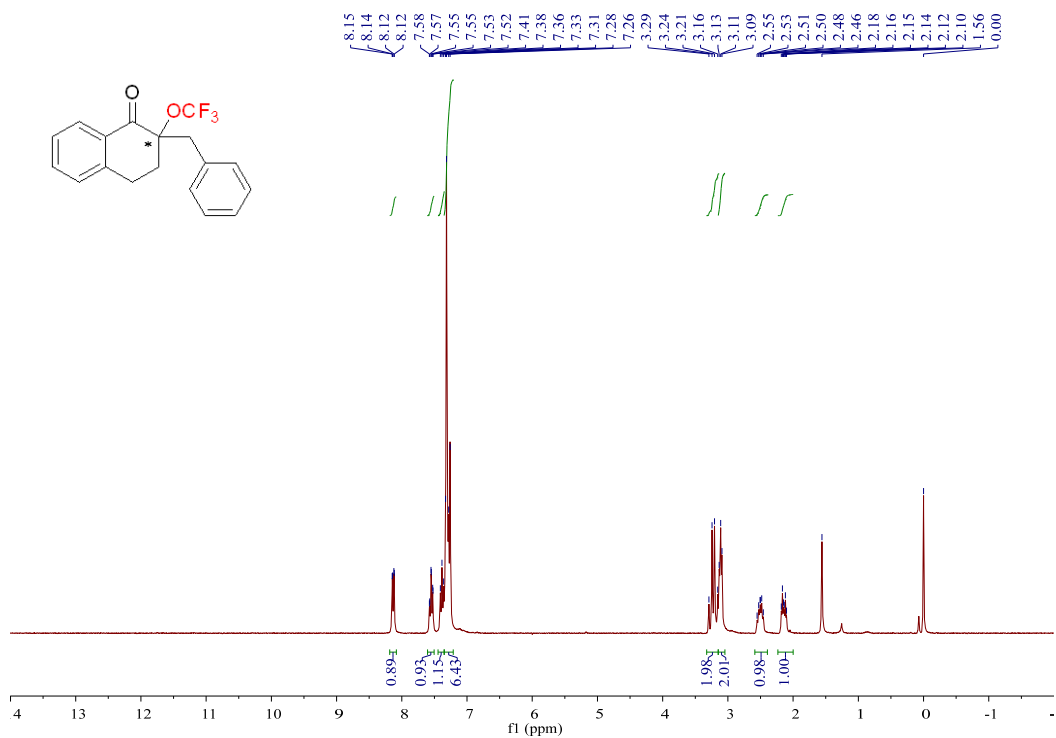


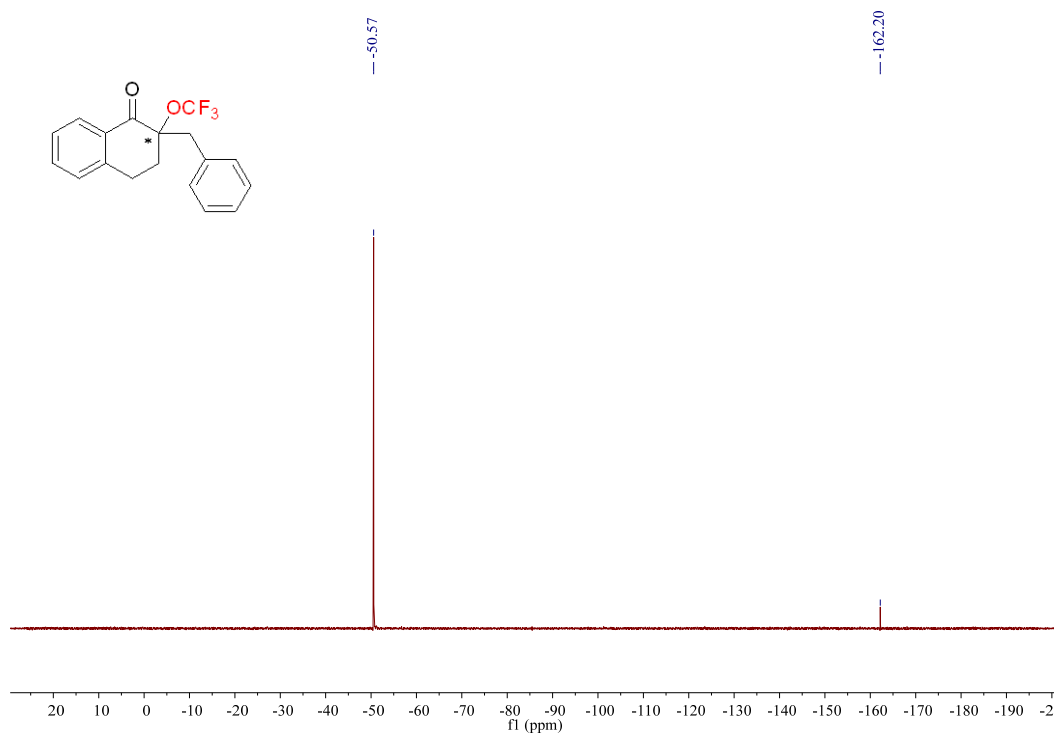
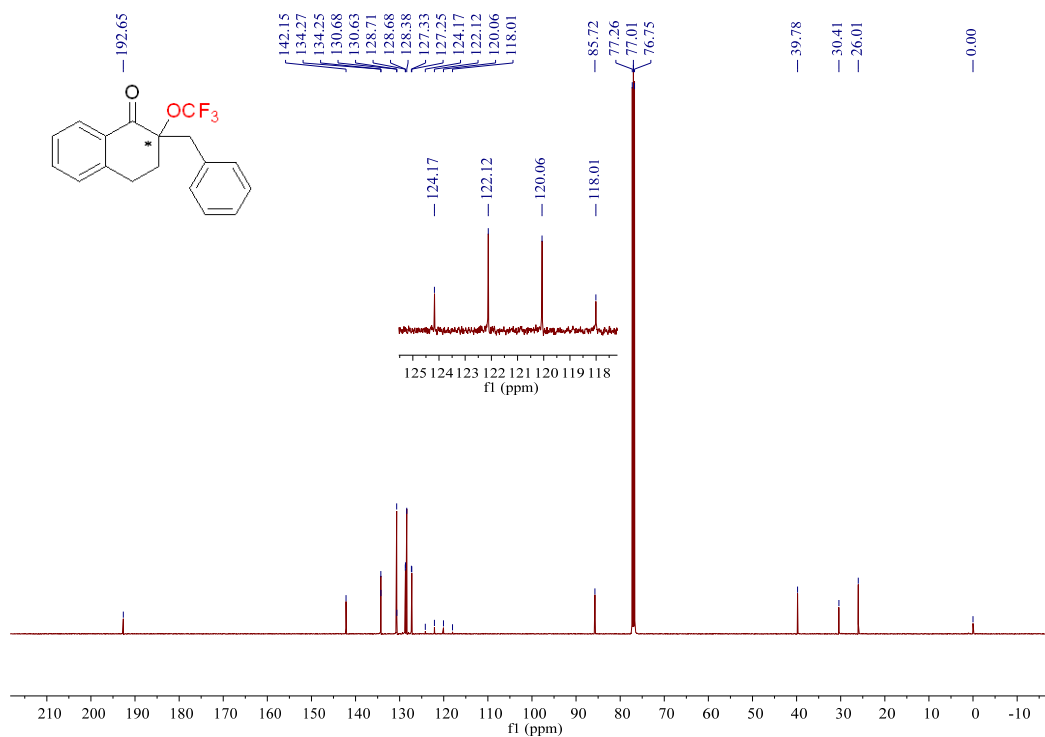
2-Benzyl-5,6-dimethoxy-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3ga**).



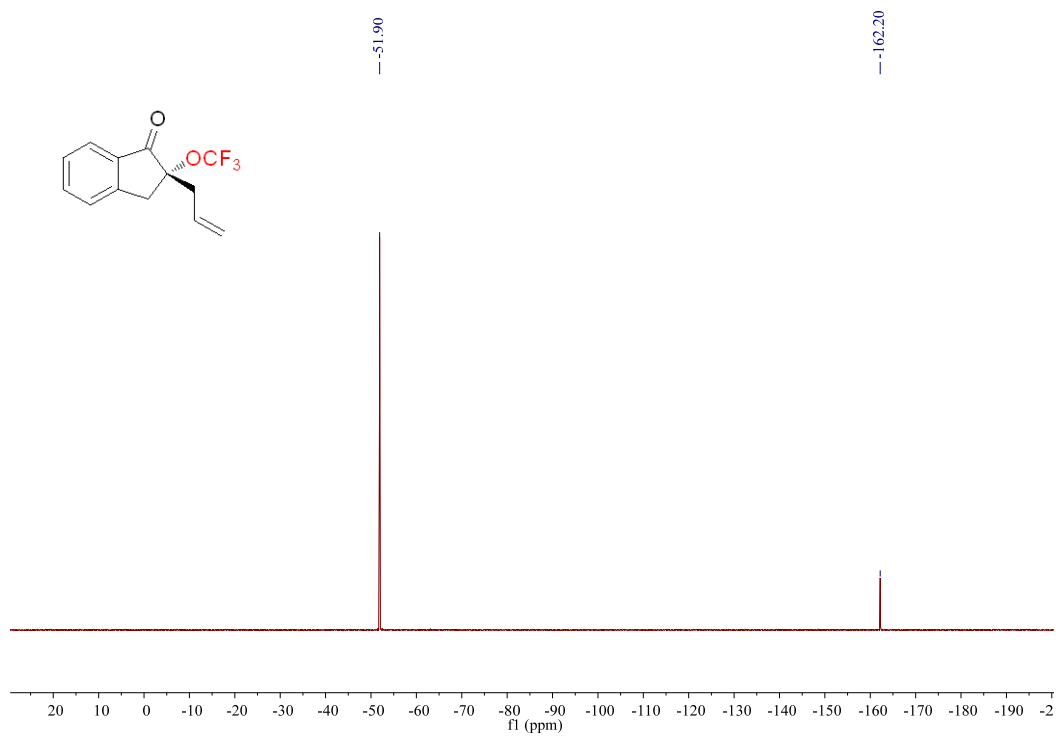
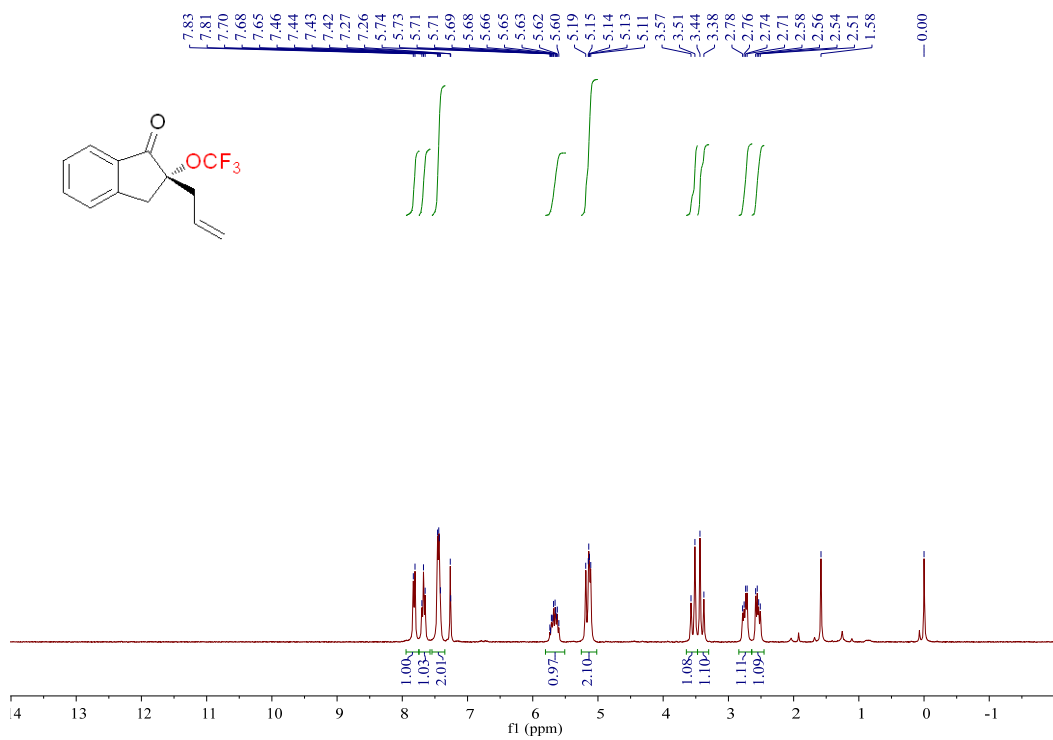


2-Benzyl-2-(trifluoromethoxy)-3,4-dihydronaphthalen-1(2H)-one (**3ha**).

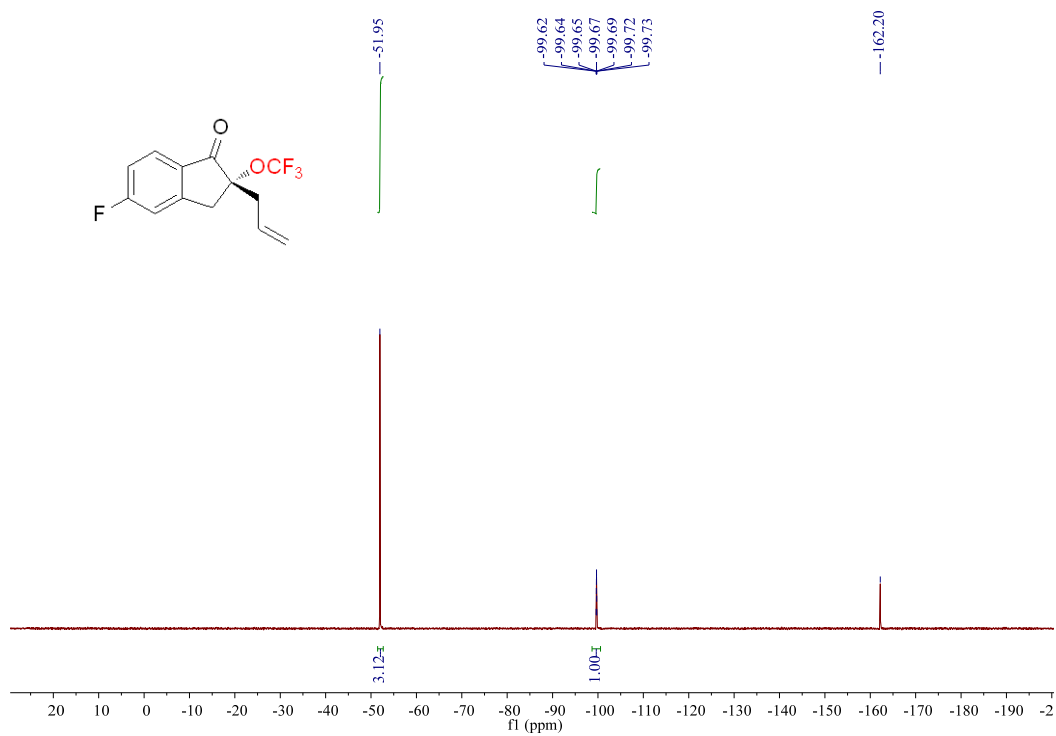
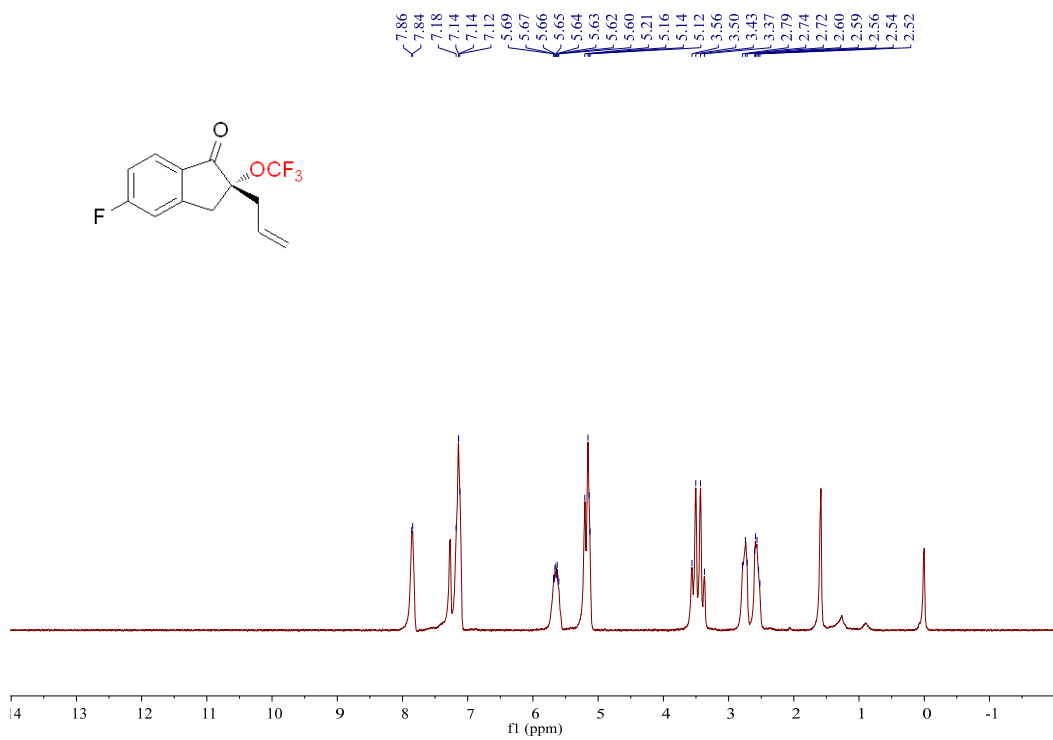




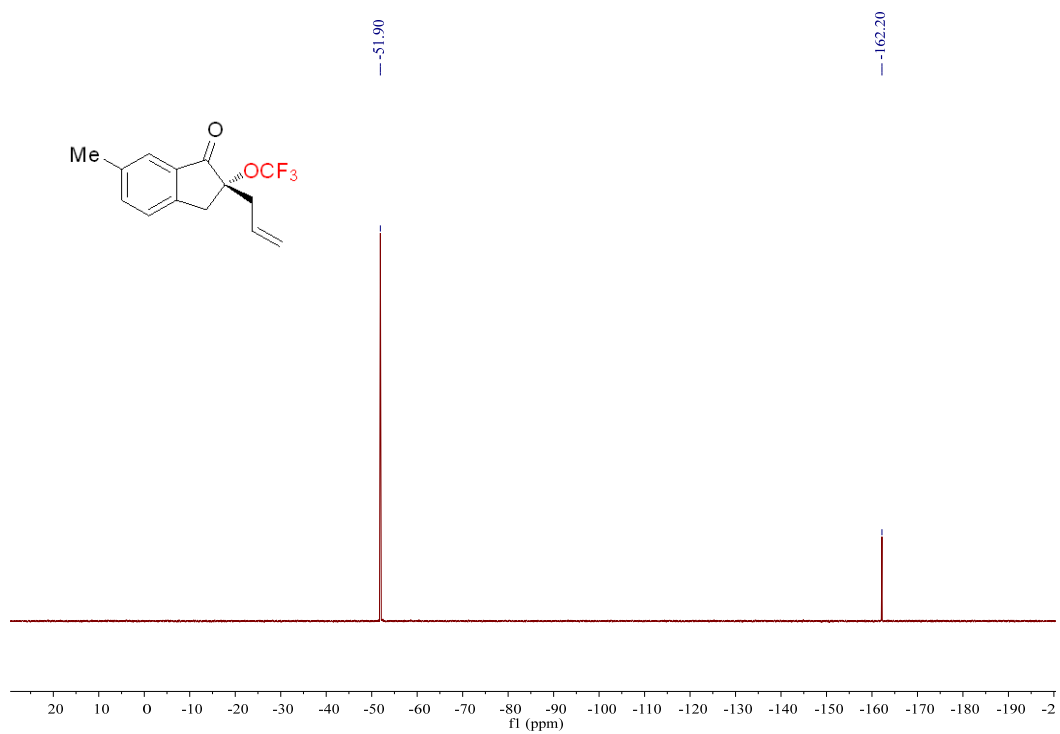
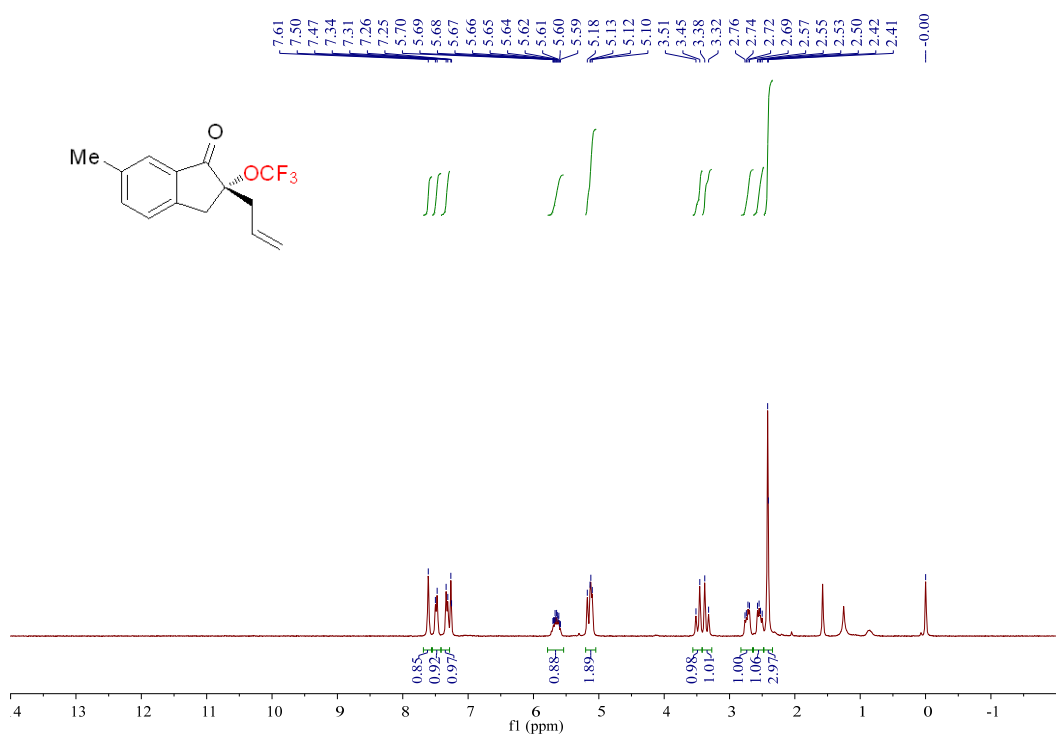
(*R*)-2-allyl-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one (**3ai**).



(R)-2-allyl-5-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3ci**)



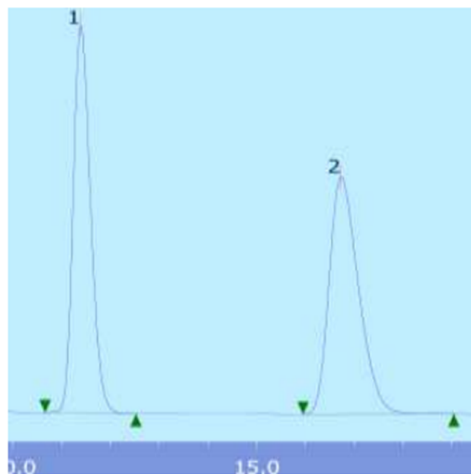
(R)-2-allyl-6-methyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one (**3ei**)



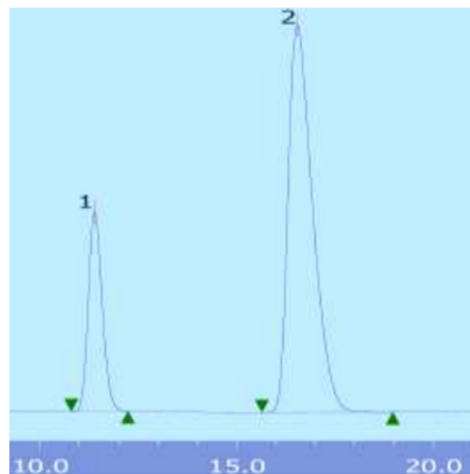
3. HPLC data for desired compounds (+)-3.

(+)-2-Benzyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3aa**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



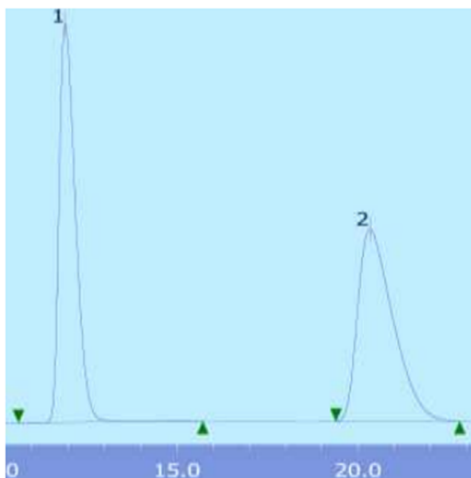
No.	tR (min)	Area (%)	Height (%)
1	11.383	49.187	62.021
2	16.725	50.813	37.979



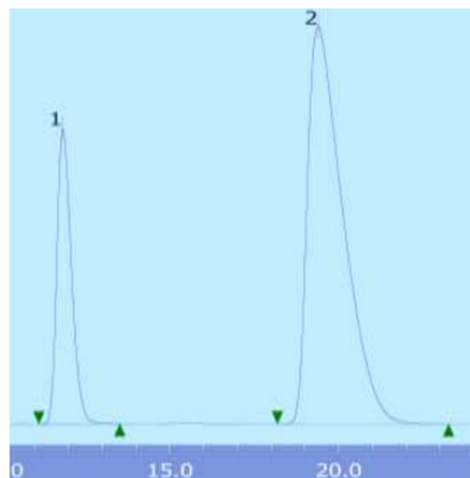
No.	tR (min)	Area (%)	Height (%)
1	11.367	22.951	34.028
2	16.525	77.049	65.972

(+)-2-(4-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3ab**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



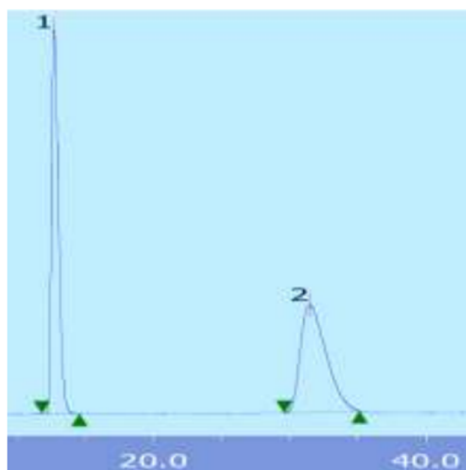
No.	tR (min)	Area (%)	Height (%)
1	11.917	49.041	67.456
2	20.325	50.959	32.544



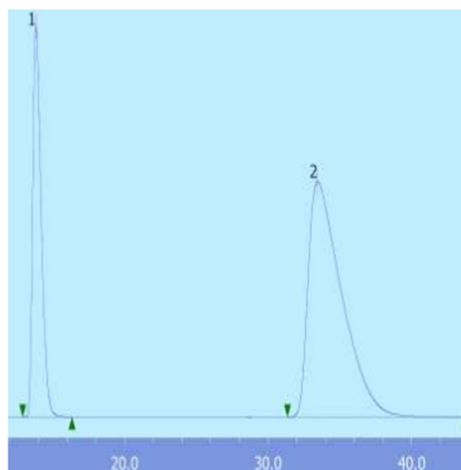
No.	tR (min)	Area (%)	Height (%)
1	11.833	23.329	42.583
2	19.383	76.671	57.417

(+)-2-(4-Bromobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3ac**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



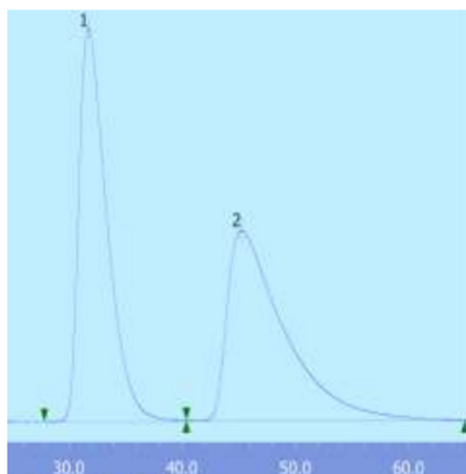
No.	tR (min)	Area (%)	Height (%)
1	12.717	49.308	78.060
2	31.458	50.692	21.940



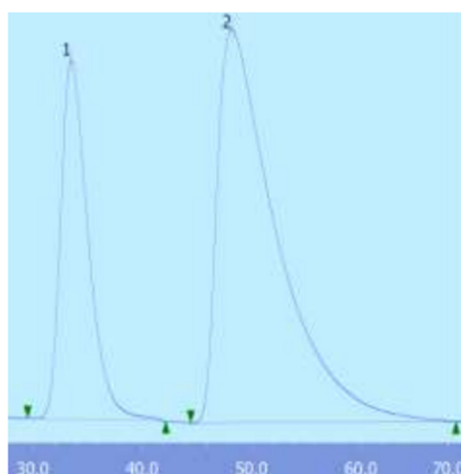
No.	tR (min)	Area (%)	Height (%)
1	13.825	29.570	62.319
2	33.433	70.430	37.681

(+)-2-(Trifluoromethoxy)-2-(4-(trifluoromethyl)benzyl)-2,3-dihydro-1H-inden-1-one ((+)-**3ad**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



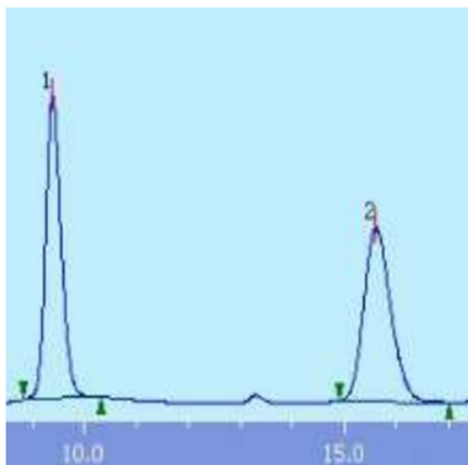
No.	tR (min)	Area (%)	Height (%)
1	31.750	50.264	67.301
2	45.242	49.736	32.699



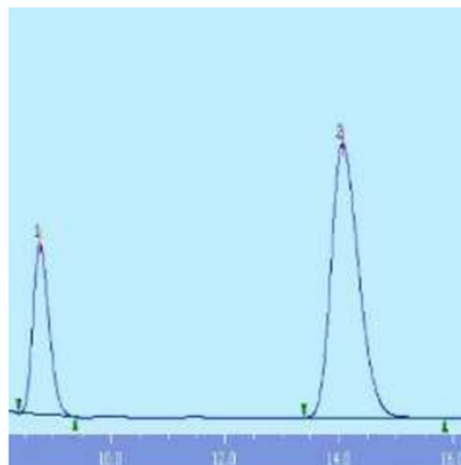
No.	tR (min)	Area (%)	Height (%)
1	33.525	29.766	47.771
2	48.208	70.234	52.229

(+)-2-(3-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3ae**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)

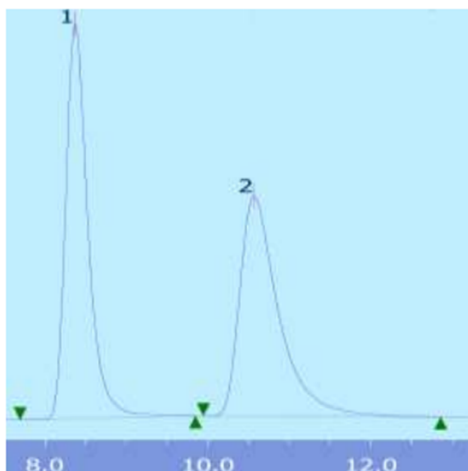


No.	tR (min)	Area (%)	Height (%)
1	9.383	50.207	63.207
2	15.592	49.793	36.529

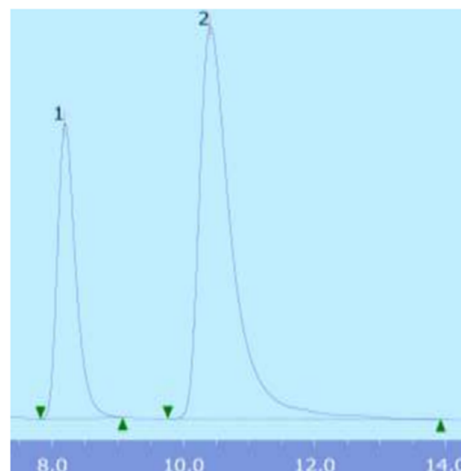


No.	tR (min)	Area (%)	Height (%)
1	8.758	26.676	38.519
2	14.050	73.324	61.481

(+)-2-([1,1'-Biphenyl]-4-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3af**).
 CHIRALPAK ID[®] column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)

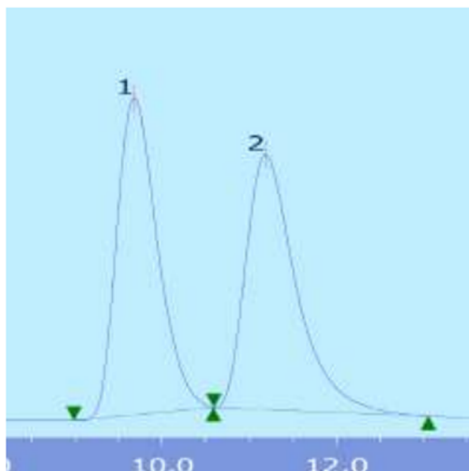


No.	tR (min)	Area (%)	Height (%)
1	8.367	50.640	64.122
2	10.567	49.360	35.878

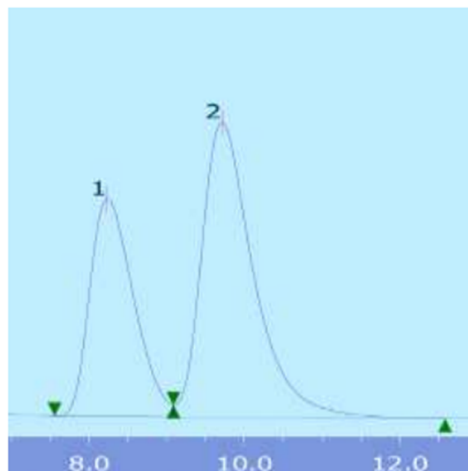


No.	tR (min)	Area (%)	Height (%)
1	8.192	29.627	42.966
2	10.408	70.373	57.034

(+)-2-(Naphthalen-2-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-**3ag**).
 CHIRALPAK[®] ID (*n*-hexane/isopropanol = 99.5/0.5, flow rate 1.0 mL/min, λ = 254 nm)



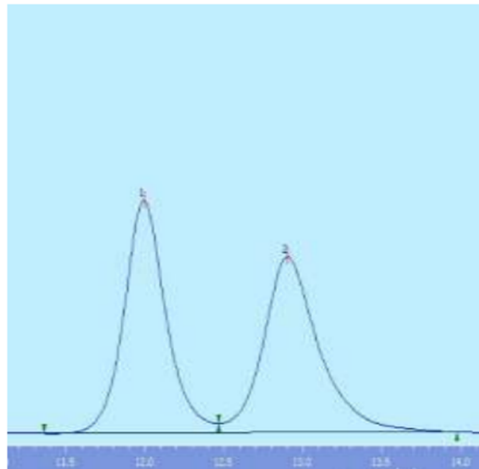
No.	tR (min)	Area (%)	Height (%)
1	9.675	50.150	55.367
2	11.183	49.850	44.633



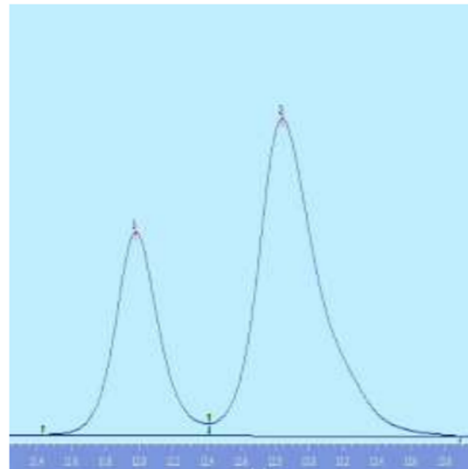
No.	tR (min)	Area (%)	Height (%)
1	8.233	38.138	42.463
2	9.708	61.862	57.537

(+)-2-(3,5-di-*tert*-butylbenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one ((+)-**3ah**).

CHIRALPAK® IF column (*n*-hexane/TBME = 95.0/5.0, flow rate 0.5 mL/min, λ = 254 nm)



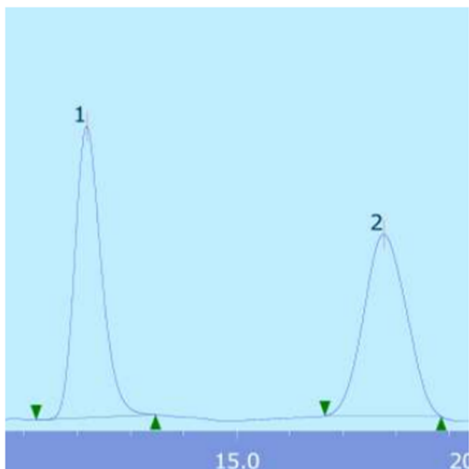
No.	tR (min)	Area (%)	Height (%)
1	11.992	49.919	56.937
2	12.900	50.081	43.063



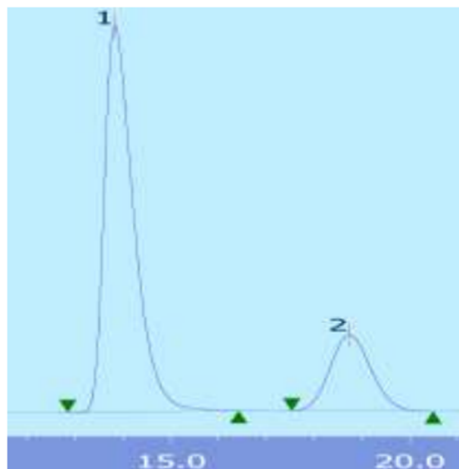
No.	tR (min)	Area (%)	Height (%)
1	11.975	31.740	39.064
2	12.842	68.260	60.936

(+)-2-Benzyl-5-bromo-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one ((+)-**3ba**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



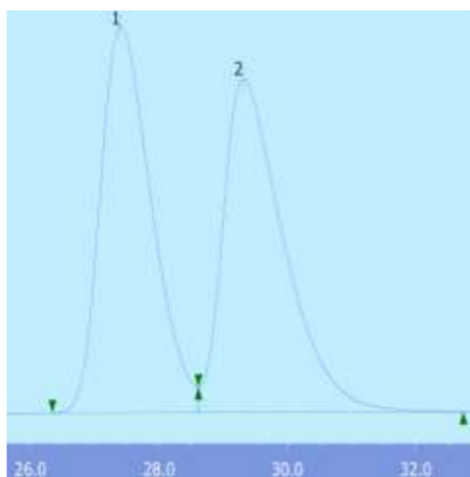
No.	tR (min)	Area (%)	Height (%)
1	12.175	49.783	61.516
2	17.758	50.217	38.484



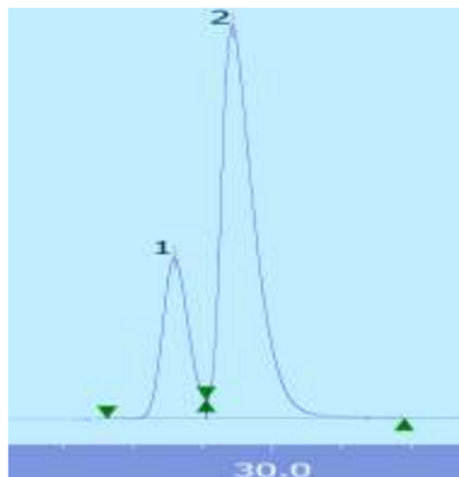
No.	tR (min)	Area (%)	Height (%)
1	13.833	78.513	83.559
2	18.725	21.487	16.441

(+)-2-Benzyl-5-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-3ca).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



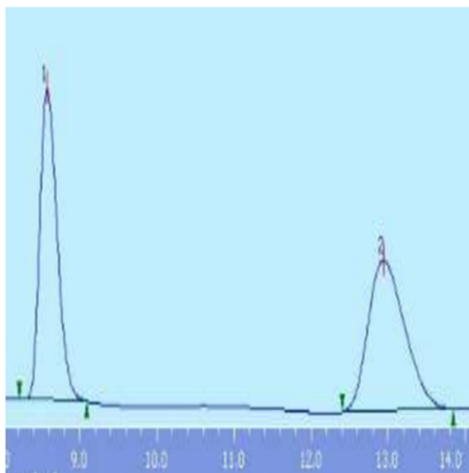
No.	tR (min)	Area (%)	Height (%)
1	27.400	49.349	53.689
2	29.317	50.651	46.311



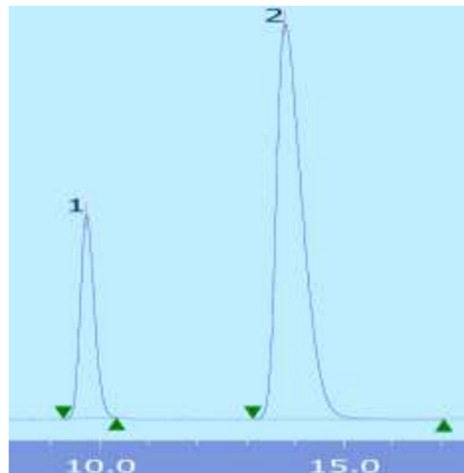
No.	tR (min)	Area (%)	Height (%)
1	27.167	24.458	29.102
2	28.833	75.542	70.898

(+)-2-Benzyl-6-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-3da).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



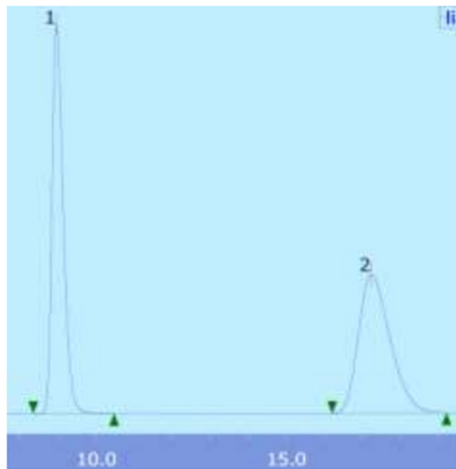
No.	tR (min)	Area (%)	Height (%)
1	8.575	49.214	67.417
2	12.925	50786	32.583



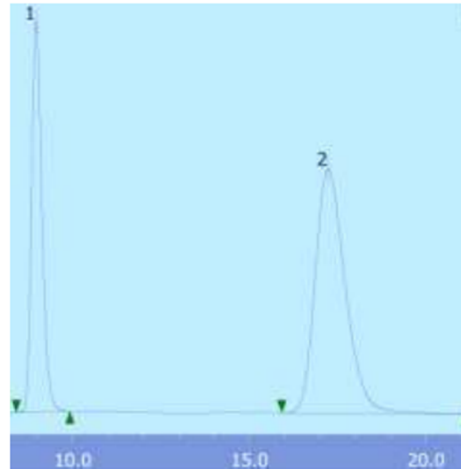
No.	tR (min)	Area (%)	Height (%)
1	9.725	21.894	33.692
2	13.792	78.106	66.038

(+)-2-Benzyl-6-methyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-3ea).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



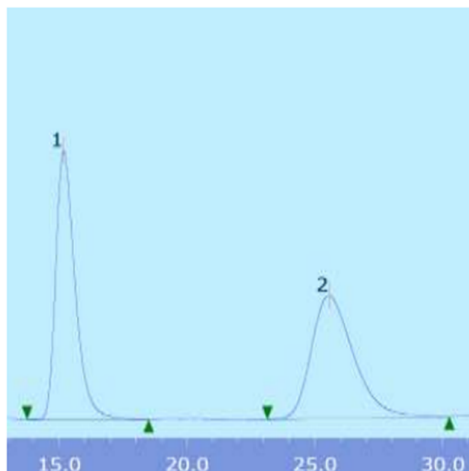
No.	tR (min)	Area (%)	Height (%)
1	8.950	49.592	73.600
2	17.233	50.408	26.400



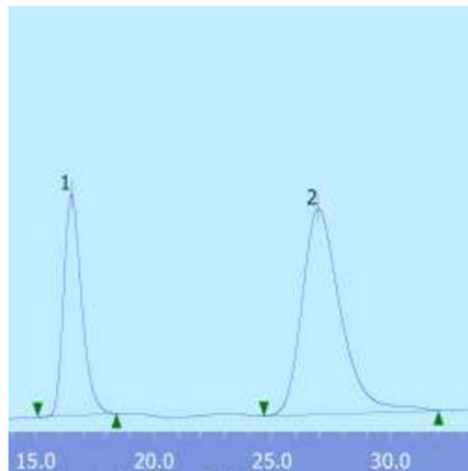
No.	tR (min)	Area (%)	Height (%)
1	8.958	35.360	61.540
2	17.217	64.640	38.460

(+)-2-Benzyl-6-methoxy-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-3fa).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



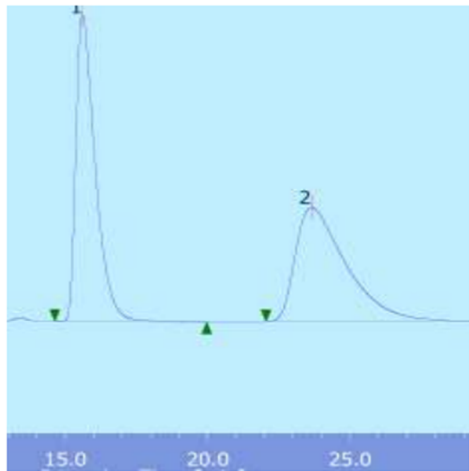
No.	tR (min)	Area (%)	Height (%)
1	15.167	50.070	68.488
2	25.533	49.930	31.512



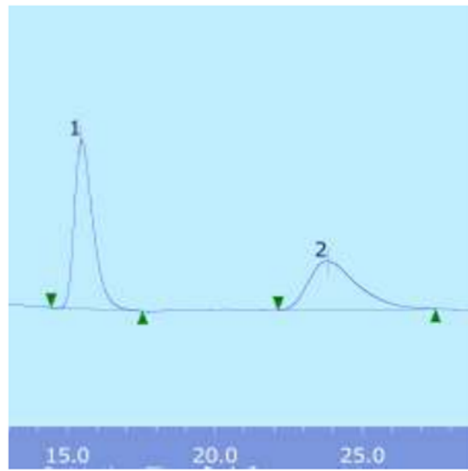
No.	tR (min)	Area (%)	Height (%)
1	16.517	33.379	51.837
2	26.942	66.621	48.163

(+)-2-Benzyl-5,6-dimethoxy-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((+)-3ga).

A series of CHIRALPAK® IF and CHIRALPAK® IA-3 (*n*-hexane/isopropanol = 90.0/10.0, flow rate 1.0 mL/min, λ = 254 nm)



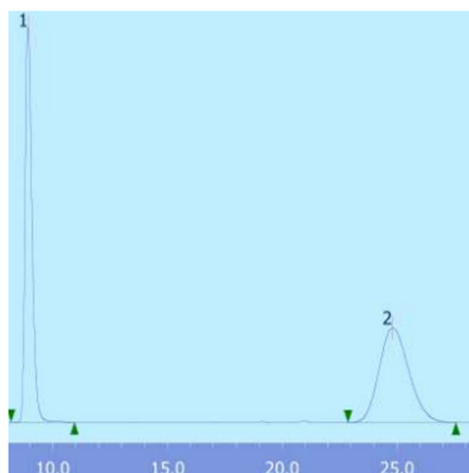
No.	tR (min)	Area (%)	Height (%)
1	15.608	50.240	72.807
2	23.642	49.760	27.193



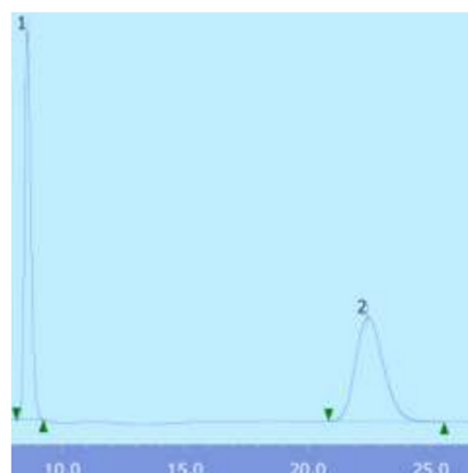
No.	tR (min)	Area (%)	Height (%)
1	15.475	56.434	77.595
2	23.808	43.566	22.405

(+)-2-Benzyl-2-(trifluoromethoxy)-3,4-dihydronaphthalen-1(2H)-one ((+)-3ha).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



No.	tR (min)	Area (%)	Height (%)
1	8.942	49.269	80.492
2	24.800	50.731	19.508

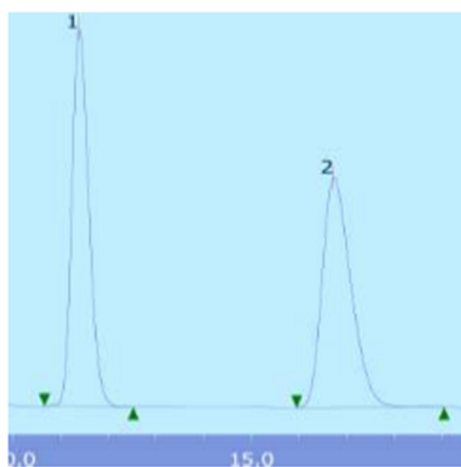


No.	tR (min)	Area (%)	Height (%)
1	8.583	46.178	78.657
2	22.442	53.822	21.343

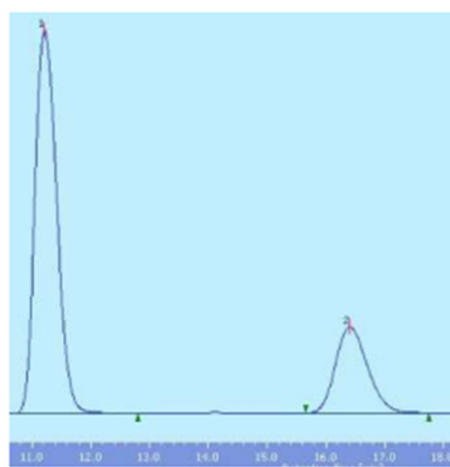
4. HPLC data for desired compounds (–)-3 in Scheme 3.

(–)-2-Benzyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((–)-**3aa**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



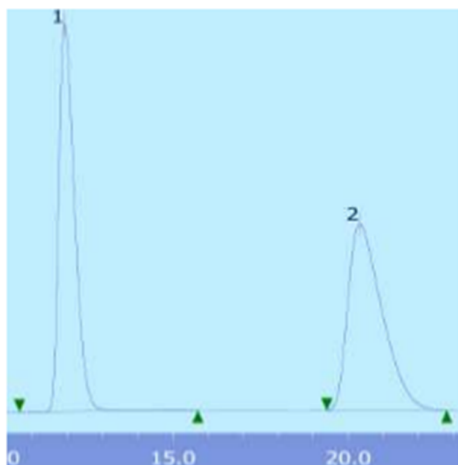
No.	tR (min)	Area (%)	Height (%)
1	11.383	49.187	62.021
2	16.725	50.813	37.979



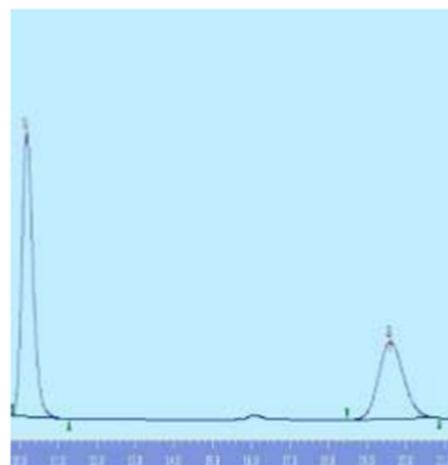
No.	tR (min)	Area (%)	Height (%)
1	11.208	75.018	81.676
2	16.400	24.982	18.324

(–)-2-(4-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((–)-**3ab**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



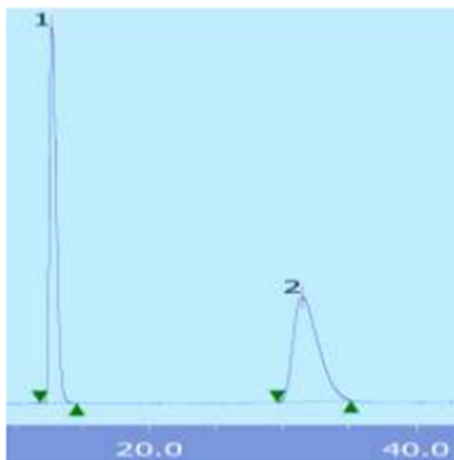
No.	tR (min)	Area (%)	Height (%)
1	11.917	49.041	67.456
2	20.325	50.959	32.544



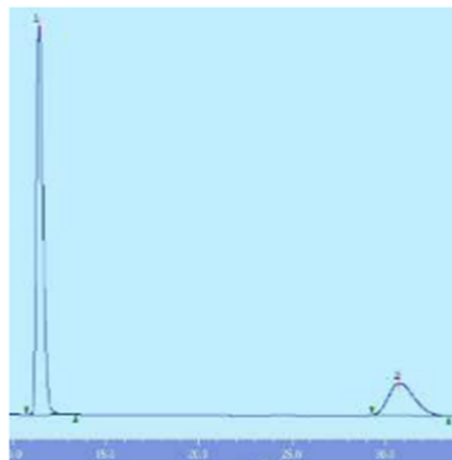
No.	tR (min)	Area (%)	Height (%)
1	11.833	62.062	78.708
2	19.383	37.938	21.292

(-)-2-(4-Bromobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((-)-**3ac**).

CHIRALCEL[®] OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



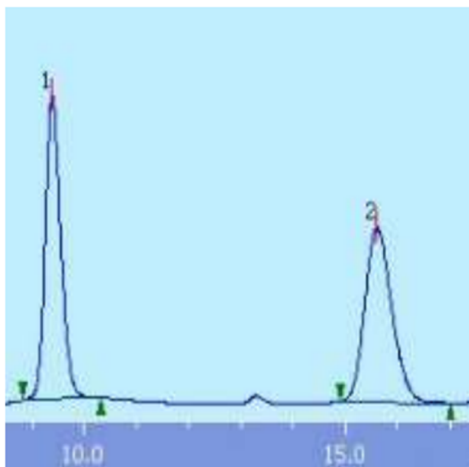
No.	tR (min)	Area (%)	Height (%)
1	12.717	49.308	78.060
2	31.458	50.692	21.940



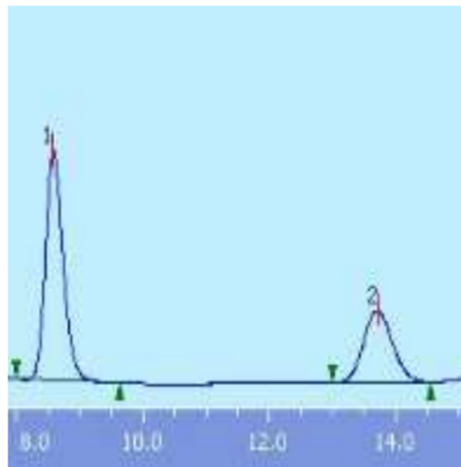
No.	tR (min)	Area (%)	Height (%)
1	11.400	75.156	92.305
2	30.725	24.844	7.695

(-)-2-(3-Fluorobenzyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((-)-**3ae**).

CHIRALCEL[®] OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)

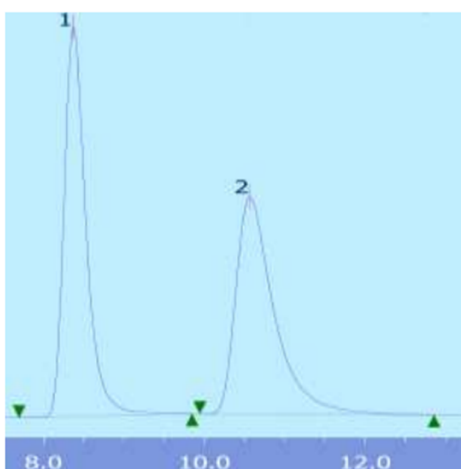


No.	tR (min)	Area (%)	Height (%)
1	9.383	50.207	63.207
2	15.592	49.793	36.529

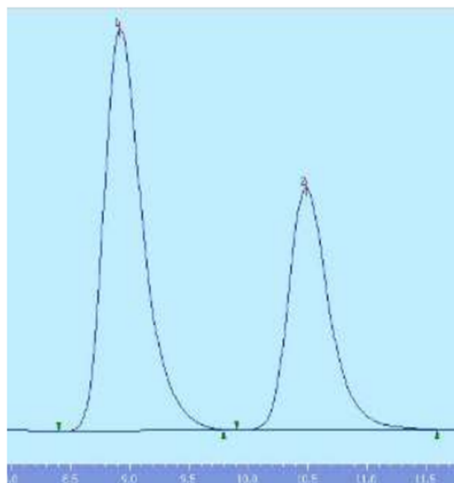


No.	tR (min)	Area (%)	Height (%)
1	8.575	65.866	75.969
2	13.708	34.134	24.031

(-)-2-([1,1'-Biphenyl]-4-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((-)-**3af**).
 CHIRALPAK ID[®] column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)

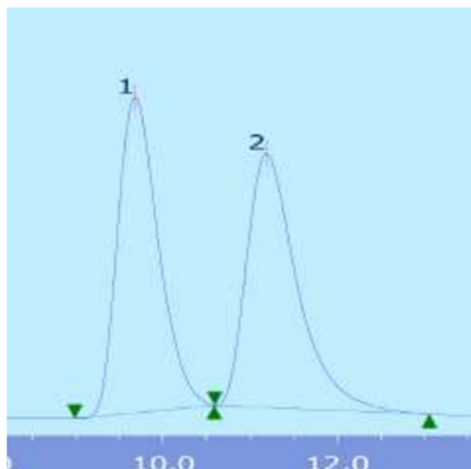


No.	tR (min)	Area (%)	Height (%)
1	8.367	50.640	64.122
2	10.567	49.360	35.878

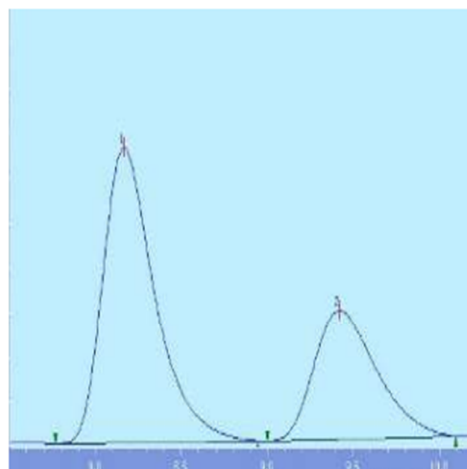


No.	tR (min)	Area (%)	Height (%)
1	8.917	61.309	62.328
2	10.483	38.691	37.672

(-)-2-(Naphthalen-2-ylmethyl)-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((-)-**3ag**).
 CHIRALPAK[®] ID (*n*-hexane/isopropanol = 99.5/0.5, flow rate 1.0 mL/min, λ = 254 nm)



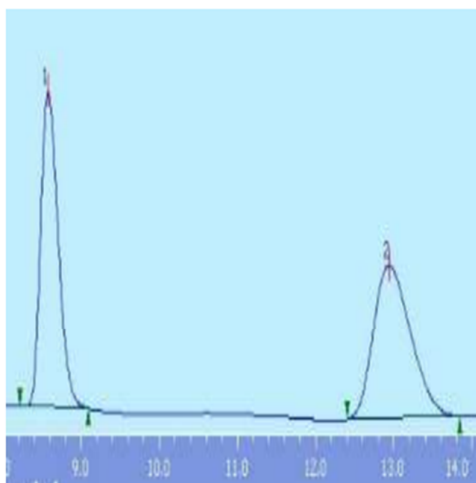
No.	tR (min)	Area (%)	Height (%)
1	9.675	50.150	55.367
2	11.183	49.850	44.633



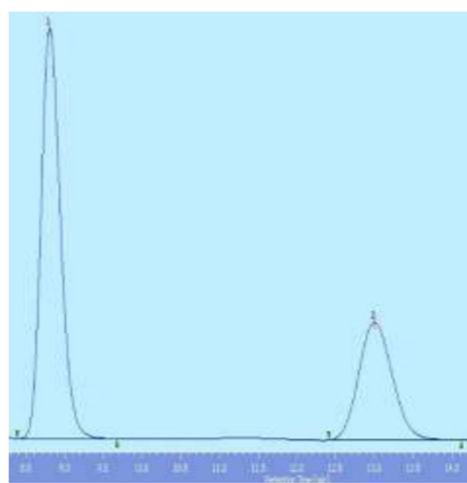
No.	tR (min)	Area (%)	Height (%)
1	8.167	65.542	69.616
2	9.417	34.458	30.384

(-)-2-Benzyl-6-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((-)-**3da**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 99.0/1.0, flow rate 1.0 mL/min, λ = 254 nm)



No.	tR (min)	Area (%)	Height (%)
1	8.575	49.214	67.417
2	12.925	50.786	32.583

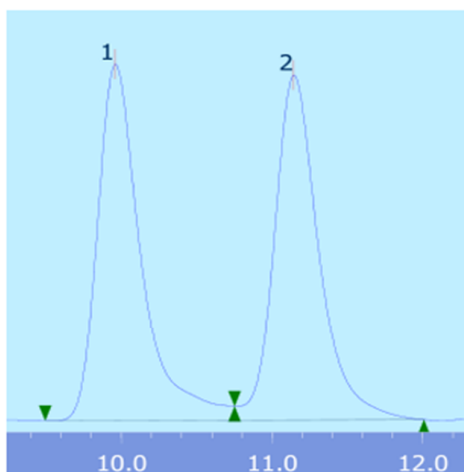


No.	tR (min)	Area (%)	Height (%)
1	8.800	66.836	77.697
2	12.992	33.164	22.303

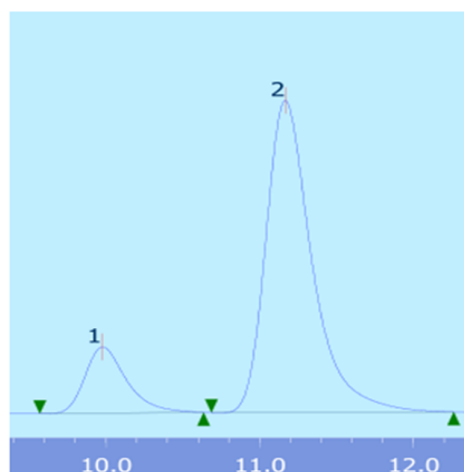
5. HPLC data for desired compounds **3** in Scheme 4.

(*R*)-2-allyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((*R*)-**3ai**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 98.0/2.0, flow rate 0.5 mL/min, λ = 254 nm)



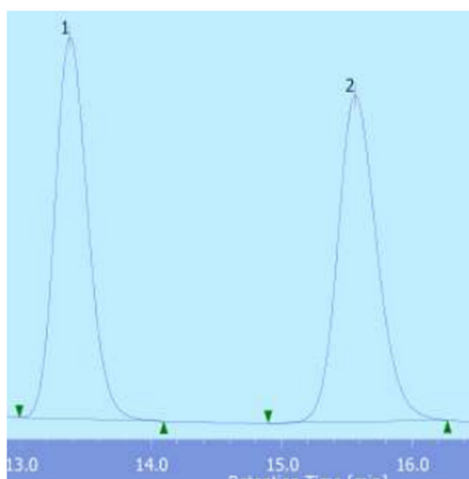
No.	tR (min)	Area (%)	Height (%)
1	9.958	50.392	50.795
2	11.142	49.608	49.205



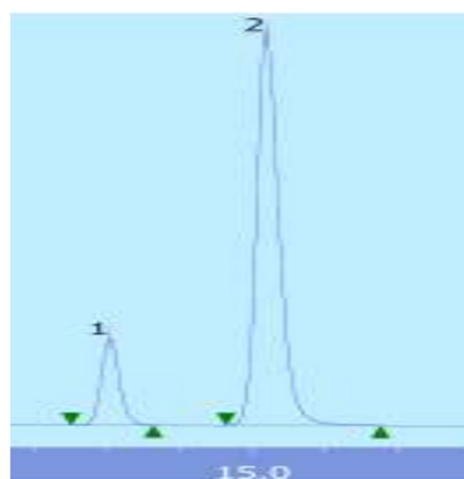
No.	tR (min)	Area (%)	Height (%)
1	9.975	16.072	17.500
2	11.167	83.928	82.500

(R)-2-allyl-5-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((*R*)-**3ci**).

CHIRALPAK® IF column (*n*-hexane/TBME = 90.0/10.0, flow rate 0.5 mL/min, λ = 254 nm)



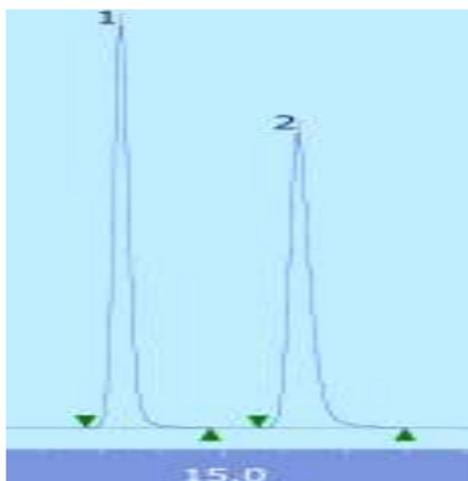
No.	tR (min)	Area (%)	Height (%)
1	13.375	49.408	53.884
2	15.558	50.592	46.116



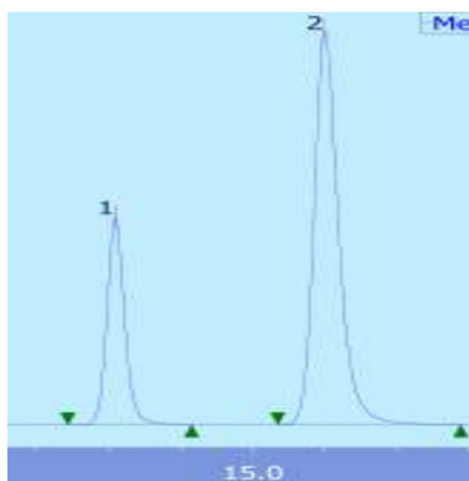
No.	tR (min)	Area (%)	Height (%)
1	13.042	14.916	18.121
2	15.192	85.084	81.879

(R)-2-allyl-6-methyl-2-(trifluoromethoxy)-2,3-dihydro-1H-inden-1-one ((*R*)-**3ei**).

CHIRALPAK® IF column (*n*-hexane/TBME = 90.0/10.0, flow rate 0.5 mL/min, λ = 254 nm)



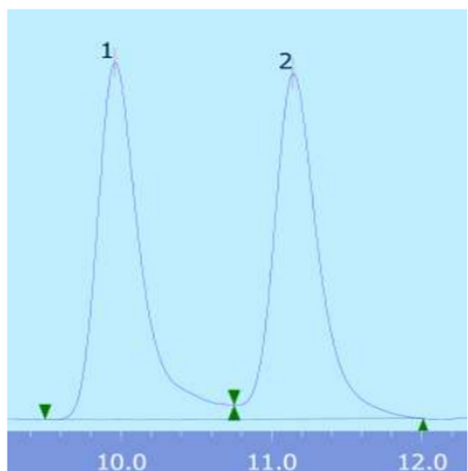
No.	tR (min)	Area (%)	Height (%)
1	13.317	49.678	57.681
2	16.217	50.322	42.319



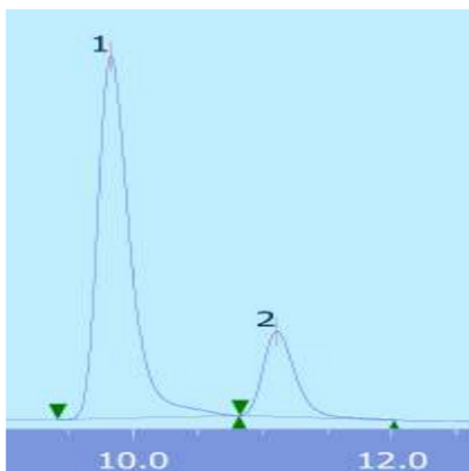
No.	tR (min)	Area (%)	Height (%)
1	13.083	27.491	34.493
2	15.992	72.509	65.507

(*S*)-2-allyl-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one (**S-3ai**).

CHIRALCEL® OJ-H column (*n*-hexane/isopropanol = 98.0/2.0, flow rate 0.5 mL/min, λ = 254 nm)



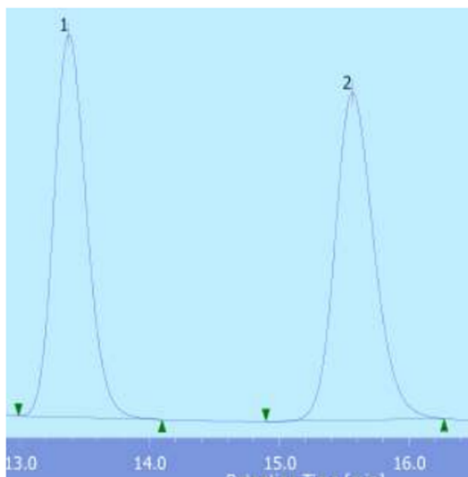
No.	tR (min)	Area (%)	Height (%)
1	9.958	50.392	50.795
2	11.142	49.608	49.205



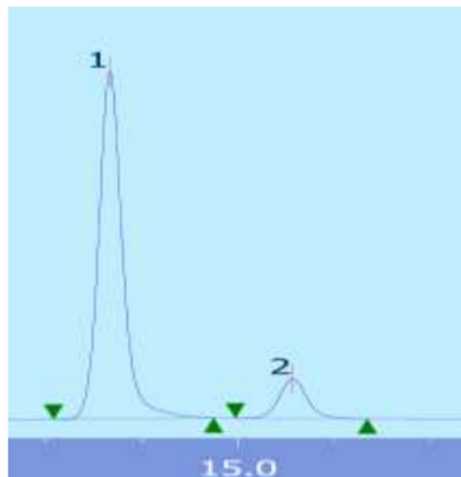
No.	tR (min)	Area (%)	Height (%)
1	9.833	81.138	80.907
2	11.108	18.862	19.093

(*S*)-2-allyl-5-fluoro-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one (**S-3ci**).

CHIRALPAK® IF column (*n*-hexane/TBME = 90.0/10.0, flow rate 0.5 mL/min, λ = 254 nm)



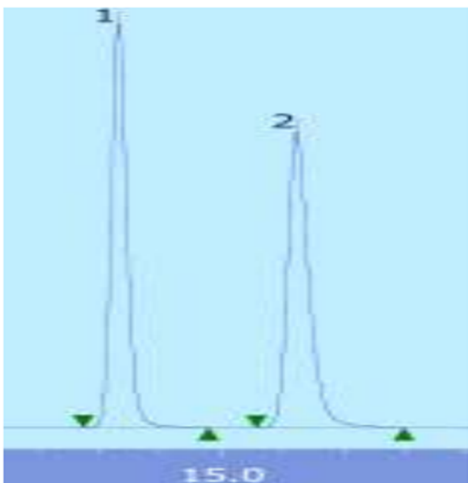
No.	tR (min)	Area (%)	Height (%)
1	13.375	49.408	53.884
2	15.558	50.592	46.116



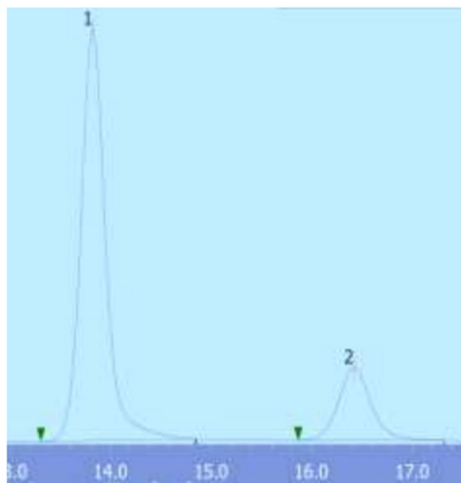
No.	tR (min)	Area (%)	Height (%)
1	13.658	88.146	89.726
2	15.567	11.854	10.274

(*S*)-2-allyl-6-methyl-2-(trifluoromethoxy)-2,3-dihydro-1*H*-inden-1-one (***S*-3ei**).

CHIRALPAK® IF column (*n*-hexane/TBME = 90.0/10.0, flow rate 0.5 mL/min, λ = 254 nm)



No.	tR (min)	Area (%)	Height (%)
1	13.317	49.678	57.681
2	16.217	50.322	42.319



No.	tR (min)	Area (%)	Height (%)
1	13.825	81.067	85.009
2	16.425	18.933	14.991